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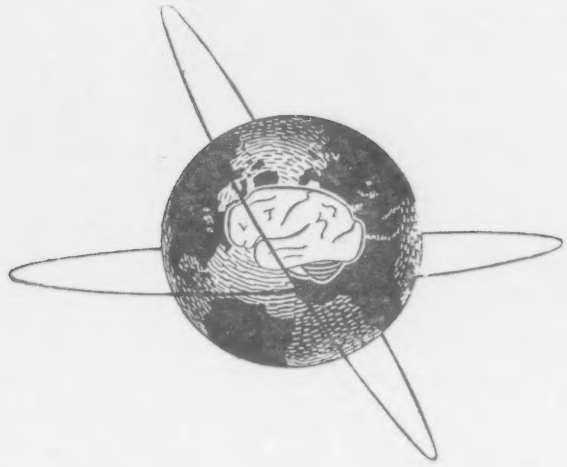
CLINICAL NEUROPHYSIOLOGY

AN INTERNATIONAL JOURNAL



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LE RÔLE DES AFFÉRENCES DES NERFS CRÂNIENS DANS LE MAINTIEN DE L'ÉTAT VIGILE DE LA PRÉPARATION "ENCÉPHALE ISOLÉ" [1]

A. ROGER [2], G. F. ROSSI [3] et A. ZIRONDOLI [4]
Istituto di Fisiologia dell'Università di Pisa, Italy

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INTRODUCTION

Le concept actuel du mécanisme du sommeil ou du maintien de l'état vigile découle des expériences de Bremer (1935, 1936) sur les effets de la section du tronc cérébral à divers niveaux, et des travaux de Moruzzi et Magoun (1949), Lindsley, Bowden et Magoun (1949), Lindsley, Schreiner, Knowles et Magoun (1950) sur le système réticulé ascendant, dont les impulsions sont transmises de façon diffuse au cortex par une voie différente de celles lemniscales et spinothalamiques. Les résultats de Starzl, Taylor et Magoun (1951) à propos de l'action collatérale des stimulis sensoriels sur la substance réticulée, ainsi que ceux d'Amassian (1952), von Baumgarten et Mollica (1954), Amassian et DeVito (1954) et Scheibel, Scheibel, Mollica et Moruzzi (1955), qui démontrèrent la convergence des impulsions afférentes sur l'unité réticulaire, mirent en évidence et précisèrent le rôle, déjà retenu par Bremer, des afférences sensitivo-sensorielles dans l'entretien d'un état vigile. De l'ensemble de ces travaux il ressort que le contrôle de la vigilance appartient au système réticulé ascendant, soumis à toutes les modalités sensorielles et projetant de façon diffuse sur le cortex.

Dans les présentes recherches nous avons cherché à déterminer l'importance respective, dans le mécanisme du maintien de la veille, de l'apport extrinsèque sensitivo-sensoriel et de l'activité intrinsèque de la formation réticulée ascendente. Il est connu que la préparation "encéphale isolé", dont toute la substance réticulée du tronc de l'encéphale est intacte et dont la sensibilité des membres et du tronc est supprimée, présente un état clinique et EEG de prévalence vigile. Si dans cette préparation la suppression des afférences encéphaliques entraîne le sommeil, la démonstration serait faite de la nécessité, pour maintenir la veille, d'un renforcement de l'activité du système réticulé par les afférences qui convergent à son niveau. Si cette désafférentation était inefficace pour modifier l'ac-

[1] Ce travail a bénéficié de l'aide du Consiglio Nazionale delle Ricerche et de la Rockefeller Foundation.

[2] Stagiaire à l'Institut National d'Hygiène (France). Boursière du Ministère des Affaires Etrangères Italien.

[3] Local research fellow de la Rockefeller Foundation.

[4] Assistant dans la Clinique Chirurgicale de l'Université de Pise.

tivité cérébrale, le maintien de l'état vigile devrait être considéré comme le fait d'une activité intrinsèque du système réticulé ascendant.

Rossi et Zirondoli (1954-55) ont montré qu'un syndrome électroencéphalographique et oculaire de sommeil suit une section pontine exécutée rostralement au noyau sensitif principal du trijumeau, tandis qu'une section caudale à ce noyau permet un état vigile comparable à celui de la préparation ''encéphale isolé''. Ces résultats pourraient faire admettre l'existence de propriétés ''activantes'' particulièrement intenses des structures pontines comprises entre les sections pré- et post-trigéminales. Ces propriétés sont-elles liées aux afférences de la Vème paire crânienne, ou bien à l'activité intrinsèque de la substance réticulée situé à ce niveau, où Brodal et Rossi (1955) ont mis en évidence une remarquable quantité des cellules à long axone ascendant ? Les résultats préliminaires de Rossi et Zirondoli (1955), obtenus chez le chat ''post-trigéminal'' avec section intracrânienne du nerf trijumeau, mettaient en évidence l'importance des afférences trigéminales dans le maintien de l'état vigile. Dans les présentes recherches on a cherché de confirmer ces résultats soit chez la préparation ''post-trigéminale'', soit chez la préparation ''encéphale isolé'', dans laquelle la totalité de la substance réticulée est en relation avec les centres supérieurs. Des expériences ont également été faites sur des préparations ''encéphale isolé'' afin de voir si la suppression des autres afférences encéphaliques a les mêmes effets que ceux consécutifs à la suppression des voies trigéminales.

TECHNIQUE

Parmis 51 chats adultes ayant été soumis à une investigation EEG, seuls 43 ont été retenus pour notre étude; les 8 autres ne satisfaisaient pas aux critères que nous nous étions imposés, c'est-à-dire: absence d'activités électroencéphalographiques pathologiques (ondes convulsives, dépression généralisée), diamètre pupillaire normal, réflexe cornéal présent, réaction d'éveil normale lorsque l'animal dormait. Des 43 expériences sur lesquelles est basé notre étude 28 ont été effectuées en ''préparation aiguë'' et 15 en ''préparation chronique''.

Les voies d'abord utilisées dans les interventions de section des nerfs crâniens ont toujours été extradurales pour la Vème paire et extra-boîte crânienne pour les autres. Les opérations étaient conduites sous anesthésie légère à l'éther. L'intervention sur les *voies trigéminales* consistait en une électrocoagulation des ganglions de Gasser: une trépanation de l'os temporal, permettant de soulever avec prudence le lobe, a été la voie d'abord extradurale que nous avons utilisée. Les *voies optiques* étaient sectionnées dans la portion immédiatement rétrobulbaire du nerf, grâce à une pénétration dans l'orbite à sa partie externe. La destruction des *nerfs acoustico-vestibulaires* était effectuée à leur origine, dans l'oreille interne, à travers le méat acoustique externe. Les *tractus olfactifs* étaient sectionnés dans leur partie prébulaire, après un effondrement des sinus frontaux. La section des *nerfs vagues* et de la *chaîne sympathique,* ainsi que l'arrachement du ganglion cervical supérieur, était permise par un dégagement des plans musculaires du cou. Un contrôle physiologique (disparition des réponses primaires) dans le cas de section des voies sensorielles, et un contrôle autopsique, dans tous les cas, ont été effectués pour s'assurer du résultat positif de ces interventions.

L'étude EEG a été réalisée chez l'animal ''encéphale isolé'' et dans 2 cas chez le chat ''post-trigéminal'' (technique décrite par Rossi et Zirondoli 1955). Les activités bioélectriques étaient dérivées soit en méthode bipolaire, soit en méthode unipolaire (référence sur la peau ou dans la partie la plus antérieure de l'os frontal) et enregistrées sur un EEGraphe Grass à 6 canaux. Les électrodes (vis) étaient fixées sur le crâne dans les régions frontale, temporale et occipitale de chaque côté. Dans quelques expériences les activités d'un des hémisphères ont été enregistrées selon la méthode électrocorticographique par l'intermédiaire d'électrodes de coton imbibées de solution physiologique et placées sur les aires corticales sensitivo-motrice, auditive et visuelle mises à nu par une petite trépanation et une dissection de la dure mère et protégées par de l'huile minérale. Dans 7

expériences chroniques les vis ont été implantés lors de l'intervention sur les nerfs, de 4 à 12 jours avant l'enregistrement.

La *méthode de travail* a été semblable, dans toutes les expériences. Dans les expériences aiguës l'évolution des activités cérébrales du chat ''post-trigéminal'' ou ''encéphale isolé'' était suivie à l'EEGraphe pendant au moins 1 heure 30′, parfois 3 heures, avant l'intervention sur les nerfs crâniens. Après celle-ci un enregistrement de 3 heures

RÉSULTATS

1) *Effets de la destruction des ganglions de Gasser sur l'activité électrique cérébrale du chat ''post-trigéminal'' ou ''encéphale isolé''.*

a) *Expériences aiguës.* Deux animaux du type ''post-trigéminal'' et cinq ''encéphale isolé'' ont été utilisés. Les ganglions de Gasser étaient détruits de 1 heure 30 min. à 3 heures après la section du névraxe. Avant la gasserectomie, le tracé EEG était constitué par des

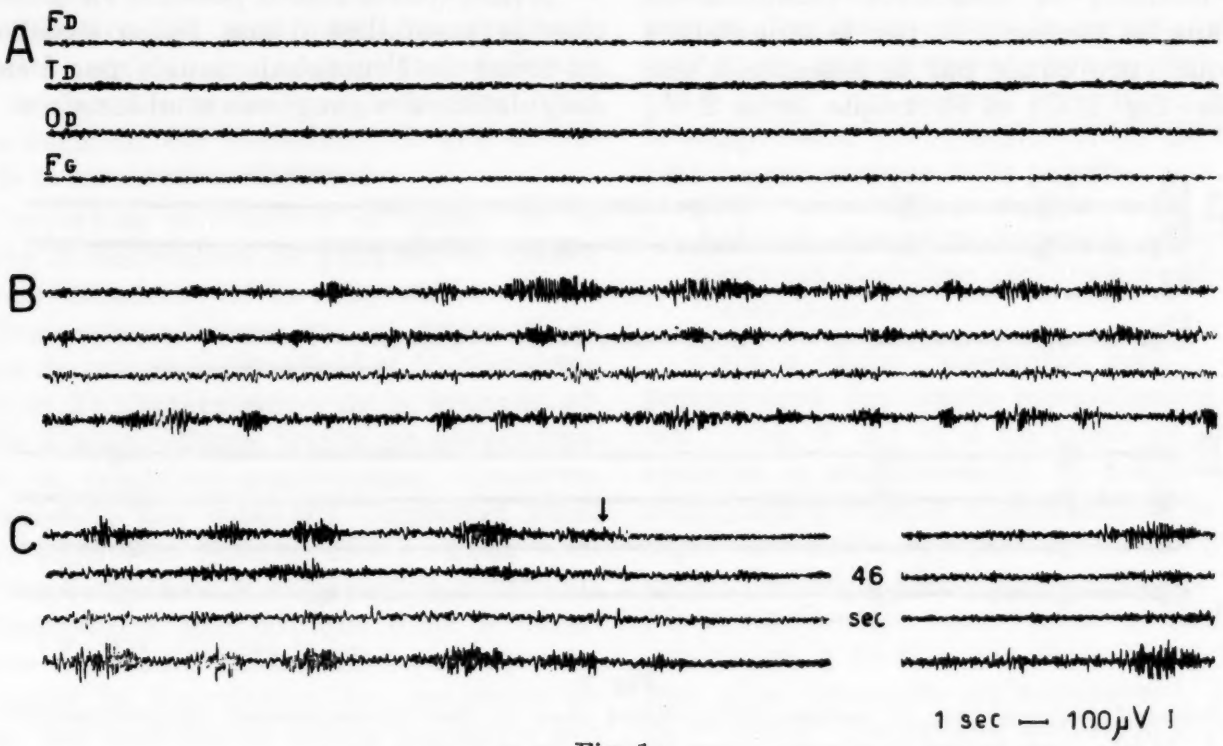

Fig. 1

Sommeil provoqué par destruction aiguë des ganglions de Gasser chez le chat postrigéminal

A. 2 heures après section du tronc cérébral: activation généralisée.
B. 30 min. après destruction des ganglions de Gasser: synchronisation générale.
C. 2 heures 45 min. après destruction des ganglions de Gasser: la flèche indique la pénétration d'une électrode dans la substance réticulée mésencéphalique et la réaction d'éveil provoquée.

(Dans cette figure et les suivantes: F = frontal, T = temporal, O = occipital, D = droit, G = gauche)

permettait d'étudier les variations du tracé. Lorsque des sections successives de différents nerfs ont été réalisées, un laps de temps d'au moins 1 heure 30′ était respecté entre chaque intervention, afin de juger des changements éventuels des rythmes cérébraux après chaque désafférentation. Dans les expériences chroniques l'enregistrement EEG, pratiqué de 4 à 12 jours après l'intervention sur les nerfs et immédiatement après section rétrobulbaire du tronc cérébral, a été dans tous les cas d'une durée de 3 heures.

rythmes rapides et de faible amplitude (fig. 1, A), très rarement interrompus par des fuseaux à 10-12 c/sec., d'amplitude supérieure à 50 μV. La pupille était mydriatique ou de diamètre normale.

La destruction des ganglions semi-lunaires entraînait dans tous les cas de nettes modifications de l'activité cérébrale. Dans les premières 30 min. suivant l'intervention s'établissait une remarquable prédominance des fuseaux d'ondes à 10-12 c/sec., d'amplitude supérieure à 50 μV., entrecoupés par des pé-

riodes d'une dizaine de secondes d'activité rapide et de basse amplitude (fig. 1, B). En même temps s'installait un myosis ''fissuré''. Bien que plus évidents dans les régions antérieures, les fuseaux d'ondes lentes étaient généralisés à toutes les dérivations. La forme du tracé ne variait pas jusqu'à la fin de l'expérience, 3 heures après la gasserectomie (fig. 1, C).

Des réactions d'éveil étaient facilement obtenues par des stimulations sensorielles açoustiques (sifflet) et olfactives (insufflation d'air dans les narines), et par la stimulation mécanique (provoquée par la descente d'une électrode: fig. 1, C) et électrique (avec 2 V., 100/sec., 1 msec.) de la substance réticulée mésencéphalique. De façon habituelle l'arousal se prolongeait quelques secondes seulement après la cessation des stimulations sensorielles, tandis qu'il persistait plus longtemps après la stimulation réticulaire.

Comme le démontre l'analyse des tracés, l'activité électrique cérébrale consécutive à la destruction des ganglions de Gasser, chez le chat ''post-trigéminal'' et ''encéphale isolé'', présente des analogies remarquables avec celle caractéristique de la préparation ''cerveau isolé'' de Bremer. Toutefois la prédominance des ''spindles'' dans les régions antérieures et surtout la facilité de provocation et la durée de l'arousal notées dans nos expériences pourrait indiquer l'existence d'une différence de degré entre le sommeil provoqué par la gasserectomie et celui obtenu dans la préparation ''cerveau isolé''.

b) ***Expériences de contrôle.*** Afin de s'assurer que les modifications des rythmes cérébraux apparues après la destruction des ganglions de Gasser étaient réellement liées à la désafférentation trigéminale et non pas à des phénomènes concomitants, des expériences de contrôle ont dû être effectuées.

Avant tout il fallait prendre en considération la possibilité d'une lésion accidentelle du tronc de l'encéphale causée par l'électrocoagulation des ganglions semi-lunaires. Bien que la possibilité de réactions d'éveil par stimulations sensorielles directement réticulaires était déjà contraire à une telle hypothèse, cinq expériences chroniques ont été effectuées. Après la destruction des ganglions de Gasser, les animaux ont survécus de 4 à 8 jours sans présenter de manifestations cliniques, autres que le syndrome périphérique d'une gasserectomie. L'enregistrement EEG exécuté après une section rétrobulbaire du névraxe, a mis en évidence chez les 5 animaux un tracé en tout point comparable à celui consécutif à une gasserectomie aiguë (fig. 2, A et B). L'examen histologique (Nissl et Weil) des coupes sériées du tronc de l'encéphale effectué dans un cas, nous a montré la complète inté-

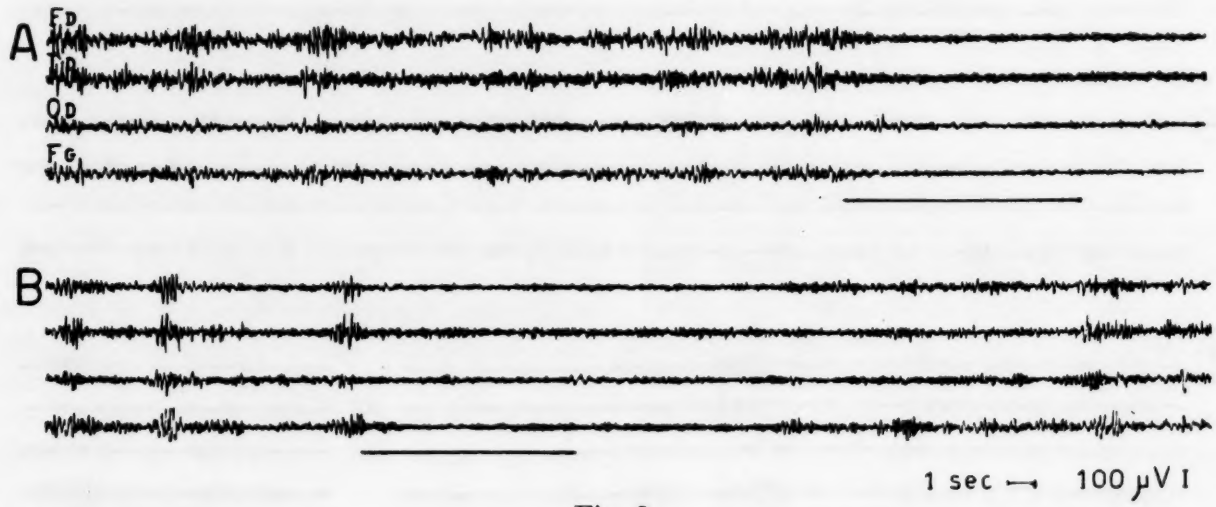

Fig. 2

Sommeil provoqué par la section rétrobulbaire chez le chat chroniquement gassérectomisé.

A. 30 min. après section du névraxe: même résultat que en B de la fig. 1.

B. 2 heures 15 min. après section du névraxe. Le trait indique une stimulation olfactive qui provoque un arousal de 14 sec.

grité anatomique du bulbe, de la protubérance, du mésencéphale et du diencéphale.

Ces expériences prouvaient l'intégrité de la substance réticulée et permettaient en même temps d'exclure le facteur irritatif lié à l'intervention aiguë. Par conséquent elles suggéraient que les modifications électroencéphalographiques produites par la gasserectomie étaient liées à la suppression de facteurs très importants pour le maintien de l'état vigile. Ces facteurs pouvaient être représentés: *a*) par la voie trigéminale extéro- et proprioceptive; *b*) mais aussi par des voies nerveuses réglant la circulation cérébrale. Dans ce dernier cas les manifestations EEG notées auraient été secondaires à une altération de la circulation cérébrale.

L'hypothèse circulatoire se basait sur le fait que la destruction du ganglion de Gasser pourrait entraîner: 1) la suppression directe de fibres sympathiques qui se trouvent au contact du ganglion (Penfield et McNaughton 1940), et 2) l'interruption de la branche afférente d'arcs réflexes trigémino-parasympathique et trigémino-sympathique, l'innervation sensitive des vaisseaux cérébraux étant liée au trijumeau (Legait 1945). Pour vérifier l'importance de la suppression éventuelle de l'innervation sympathique dans le déterminisme des modifications EEG qui apparaissent après la destruction des ganglions de Gasser, les expériences aiguës suivantes ont été réalisées. Chez 3 chats ''encéphale isolé'' la stimulation du bout périphérique de la chaîne sympathique cervicale par des impulsions rectangulaires (de 2 à 5 V., 30/sec., 5-10 msec.) était sans effet sur l'EEG, alors qu'une constriction des vaisseaux corticaux était constatée au stéréomicroscope. Dans les mêmes préparations la ganglionectomie cervicale supérieure bilatérale n'entraînait aucune modification des activités électriques cérébrales. L'hypothèse 1) peut être donc écartée. Il ne saurait s'agir d'ailleurs, dans nos expériences, de la suppression de la branche afférente de réflexes trigémino-sympathiques, car ceux-ci étaient déjà éliminés par la section sous-bulbaire. Quant aux réflexes trigémino-parasympathiques, dont la branche efférente serait représentée par les fibres autonomes du VII° (Cobb et Finesinger 1932; Chorobski et Penfield 1932; Forbes, Nason, Cobb et Wortman 1937; Darrow, Green, Davis et Garol 1944), ceux-ci étaient déjà interrompus dans nos chats post-trigéminaux dont l'EEG est pourtant tout à fait semblable à celui de la préparation ''encéphale isolé''. Tous ces contrôles permettaient donc d'exclure que les tracés EEG de sommeil produits par la gasserectomie étaient liés à des altérations circulatoires. Par conséquent la seule explication possible du phénomène était la suppression de la sensibilité trigéminale. On ne saurait en dire autant pour le myosis apparaissant après gasserectomie chez le chat ''encéphale isolé'', qui pouvait être dû en partie à la suppression post-ganglionnaire de l'innervation sympathique de la pupille.

2) *Effet de la section des nerfs optiques sur l'activité électrique cérébrale du chat ''encéphale isolé''.*

Chez 4 chats ''encéphale isolé'', dont 2 présentaient des tracés complètement ''activés'' (fig. 3, A) et 2 un tracé où quelques spindles se superposaient de temps à autre aux rythmes rapides et peu amples, la section aiguë des nerfs optiques modifiait discrètement l'activité électrique cérébrale. Après l'interruption des voies visuelles, les fuseaux généralisés à 10-12 c/sec. étaient en effet un peu plus fréquents qu'auparavant (fig. 3, B, C et D). Les stimuli acoustiques et trigéminaux déterminaient des réactions d'éveil pouvant se prolonger plusieurs minutes. Dans 5 chats la section sous-bulbaire était pratiquée de 4 à 12 jours après l'interruption bilatérale des nerfs optiques. Ces expériences chroniques confirmèrent les données recueillies en préparation aiguës en mettant en évidence des ''patterns'' EEG caractéristiques d'un état fonctionnel où l'activité vigile prédominait nettement sur celle de sommeil (fig. 4, A, B et C).

3) *Effets de la section des nerfs acoustico-vestibulaires et olfactifs sur l'activité électrique cérébrale du chat ''encéphale isolé''.*

Les résultats étant similaires après la section de la VIIIème paire crânienne (5 cas) et des tractus olfactifs (4 cas) nous les étu-

dieront dans un même paragraphe. Chez tous les animaux le tracé était ''activé'' ou discrètement synchronisé pendant toute la durée de l'enregistrement précédent l'interruption des voies acoustico-vestibulaires ou olfactives. Dans 7 cas aucune modification globale de l'activité électrique cérébrale n'a été notée pendant les 3 heures d'enregistrement consécutif à la section de ces voies. Chez 2 animaux, toutefois, l'élimination des afférences acoustico-vestibulaires fut à l'origine de quelques spindles généralisés groupés en brèves périodes, se superposant à l'activité rapide qui caractérisait le tracé avant l'intervention.

L'enregistrement effectué dans trois préparations chroniques (VIIIème paire sectionnée depuis 4 jours chez 2 animaux, et tractus olfactif interrompu depuis 6 jours dans un cas) confirma les données recueillies dans les préparations aiguës.

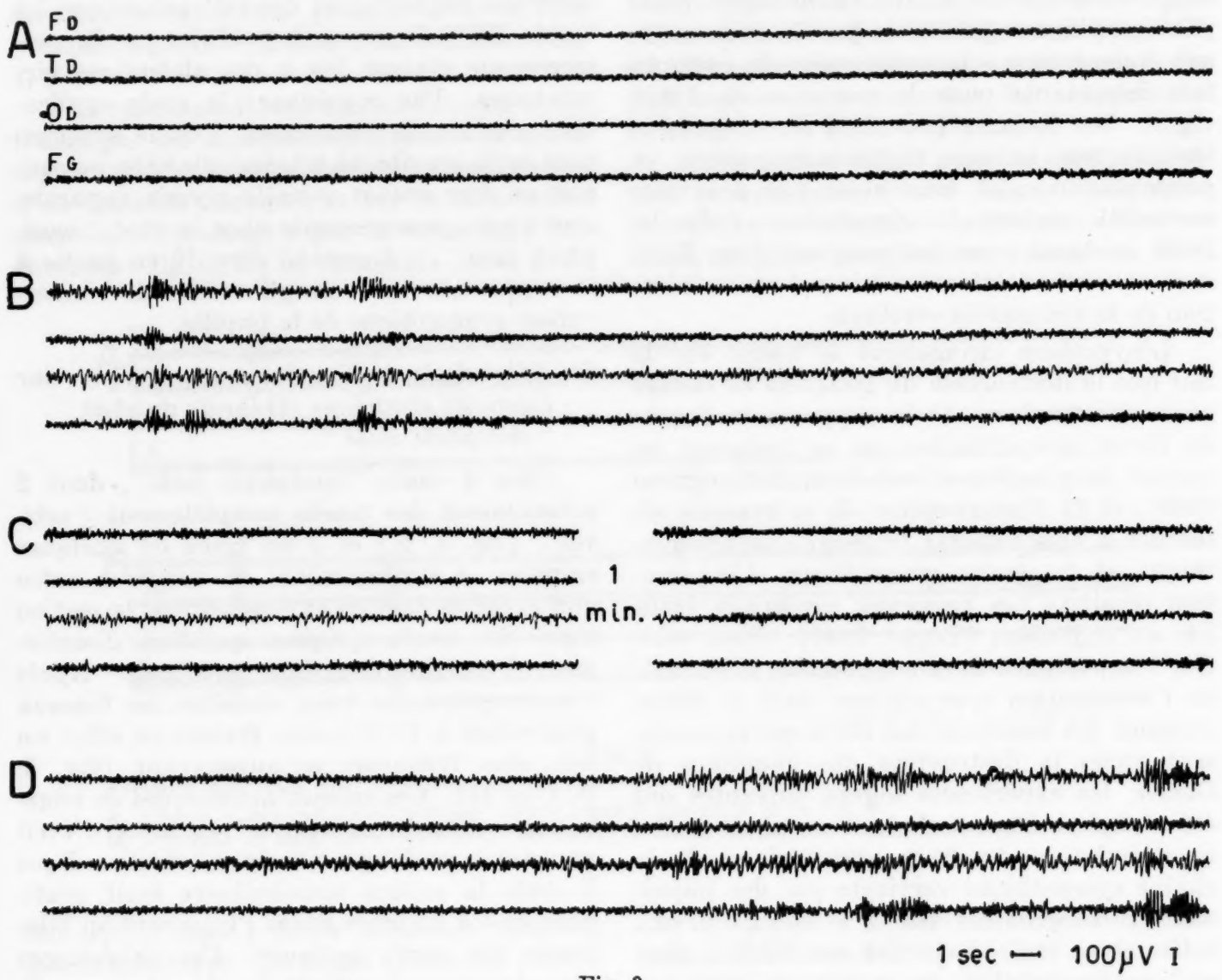

Fig. 3

Alternance de sommeil et d'éveil chez le chat ''encéphale isolé'', après section aiguë des deux nerfs optiques.

A. 1 heure après section du névraxe: activation généralisée.

B, C et D. 1 heure après section des nerfs optiques: alternance de longues périodes d'activation spontanée et de phases de synchronie lente.

4) *Effets de sections simultanées ou successives de plusieurs nerfs crâniens sur l'activité électrique cérébrale du chat ''encéphale isolé''.*

Les sections successives ont été pratiquées dans 5 expériences aiguës.

Chez un animal, la section des voies olfactives, puis, 1 h. 30′ plus tard, des voies

acoustico-vestibulaires, n'entraînait aucune modification du tracé de type ''activé'' enregistré pendant 1 h. en préparation ''encéphale isolé'' pure. L'interruption des voies optiques chez 2 chats ''encéphale isolé'' ayant déjà subi 90 min. auparavant une section, pour l'un des tractus olfactifs, et pour l'autre des nerfs acoustico-vestibulaires, a été inefficace pour provoquer les ''patterns'' EEG caractérisant un état de sommeil.

L'effet critique de l'interruption de la voie trigéminale uni- ou bilatérale a été mise en évidence dans deux expériences. Dans ces 2 préparations les sections successives de la VIIIème paire crânienne et des 2 nerfs vagues n'avaient pas transformé le tracé de type ''activé'' qui caractérisait la préparation ''encéphale isolé'' (fig. 5, A et B). L'élimination des afférences trigéminales, pratiquée simultanément dans un cas et successivement dans l'autre, a produit l'apparition de fuseaux d'ondes lentes à 10-12 c/sec. généralisés et continus (fig. 5, C et D) et du myosis. L'arousal provoqué par la stimulation olfactive et par la stimulation mécanique et électrique (2 V., 300/sec., 1 msec.) de la substance réticulée du mésencéphale, prouvait l'intégrité fonctionnelle de ces deux préparations ''encéphale isolé'' désafférentées du point de vue auditif, vestibulaire, vagal et trigéminal (fig. 5, C et D).

La section simultanée de plusieurs nerfs crâniens a été réalisée dans deux expériences chroniques. Des rythmes rapides et peu amples auquels se superposaient à intervalles irréguliers et toujours prolongés quelques fuseaux d'ondes lentes généralisés, caractérisaient les tracés provoqués par la section rétrobulbaire chez un animal anosmique et aveugle depuis 8 jours, et chez un autre ayant subit 8 jours plus tôt une section des VIIIème et IIème paire crânienne.

Les divergences frappantes existant chez le chat ''encéphale isolé'' entre les effets dû à la suppression des afférences trigéminales et les afférences des autres nerfs crâniens pourraient être liées à l'existence chez les animaux non gasserectomisés d'impulsions douloureuses naissant de régions correspondantes à la blessure médiofrontale (nécessaire à la mise en place des électrodes), qui sont en grande partie innervées par le trijumeau.

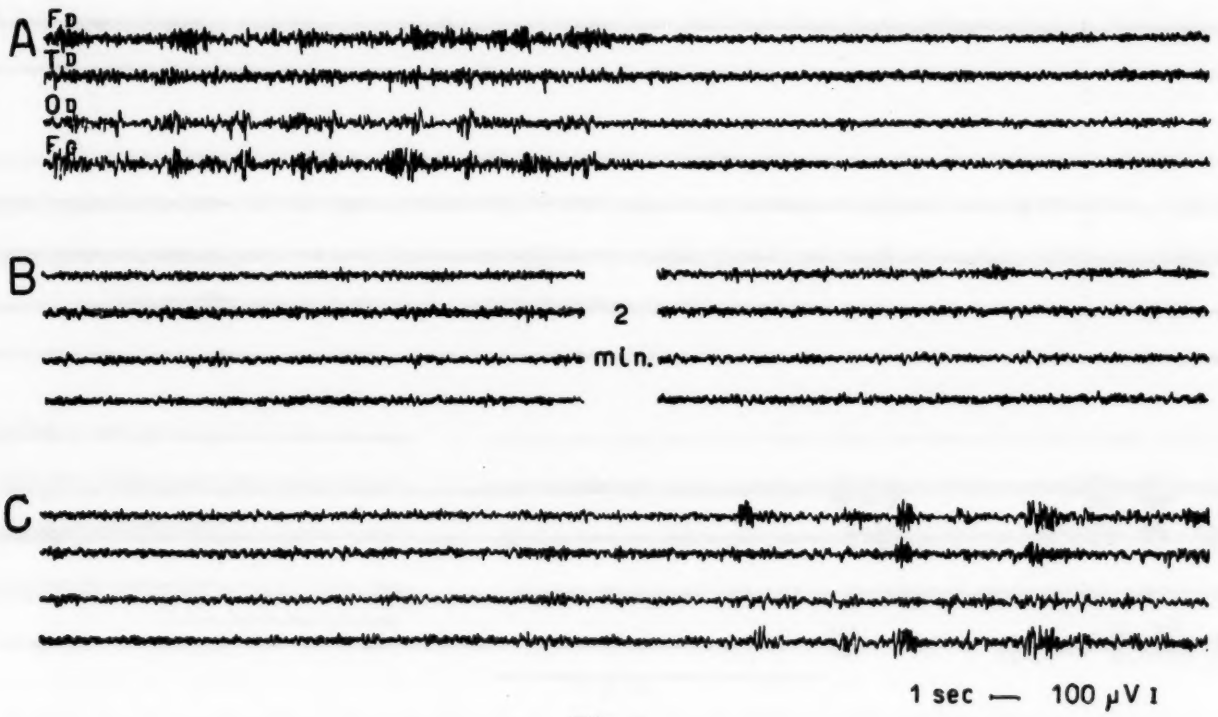

Fig. 4

Alternance de sommeil et d'éveil provoquée par la section rétrobulbaire chez le chat chroniquement privé des afférences optiques.

A, B et C. 45 min. après section à C I: mêmes résultats que en B, C et D de la fig. 3.

Cette suggestion ne peut être retenue puisque dans 7 de nos expériences chroniques (5 chats aveugles et 2 dont la VIIIème paire était sectionnée) la blessure avait été évité, les tracés ayant été enregistrés de 4 à 12 jours après l'intervention grâce à des électrodes chroniquement implantées. Dans ces conditions les tracés étaient en tout point comparable à ceux qui caractérisaient les préparations aiguës.

5) *Effet de la suppression d'une modalité sensorielle sur l'électrocorticogramme de son aire de projection spécifique.*

Les résultats que nous avons obtenu après suppression des modalités sensorielles étaient en contradiction apparente avec ceux de Claes (1939), qui avait mis en évidence l'apparition de périodes d'inactivité corticale séparées "par des groupes fusiformes d'ondes de voltage proportionnellement élevé mais de

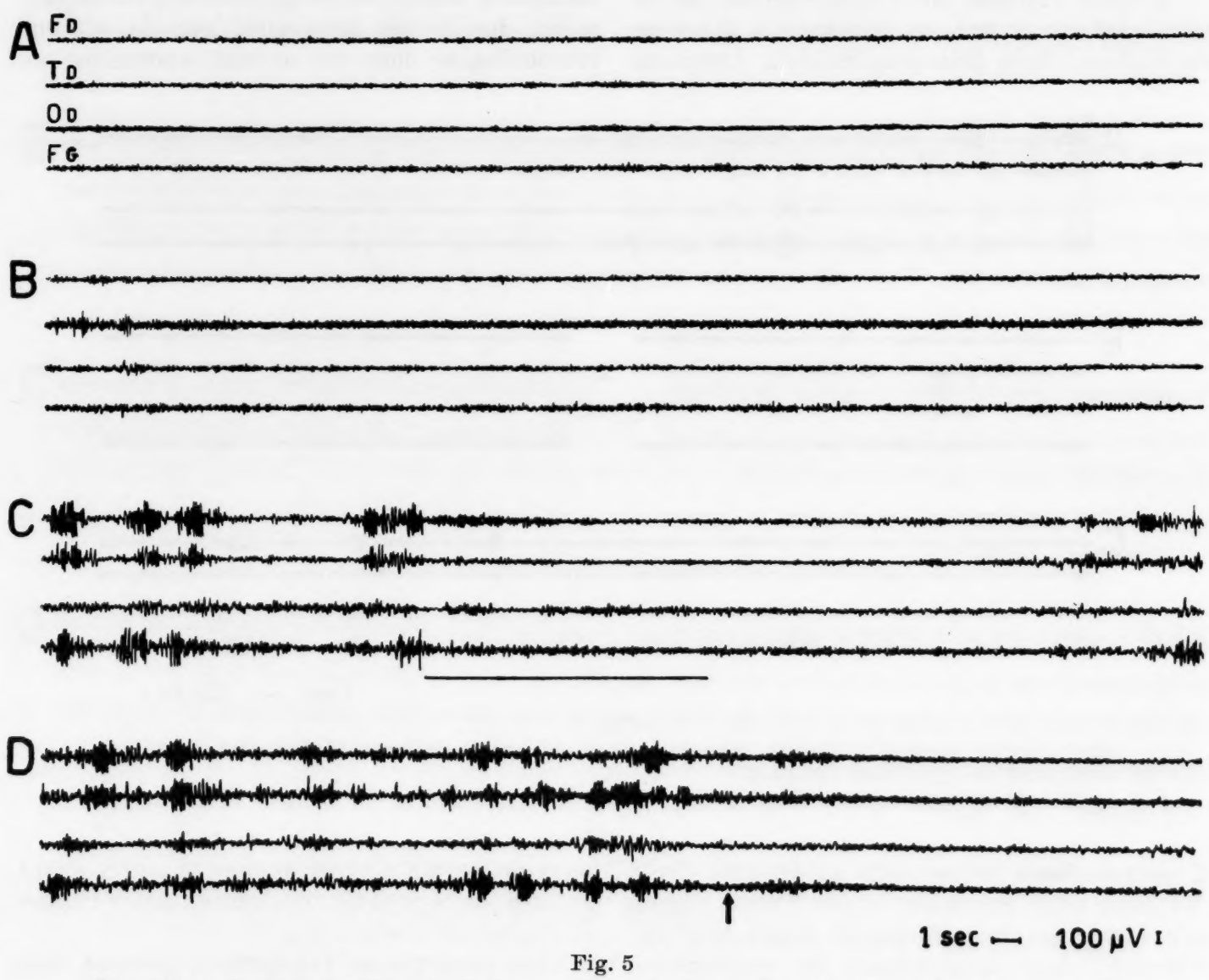

Fig. 5

Importance de la destruction aiguë des ganglions de Gasser dans la provocation du sommeil chez le chat "encéphale isolé".

A. 1 heure 45 min. après section du névraxe et immédiatement avant la section des nerfs VIII: activation généralisée.
B. 2 heures 45 min. après section des nerfs VIII et 1 heure 30 min. après section des nerfs X: même tracé que en A.
C. 15 min. après destruction du ganglion de Gasser droit: noter la présence des fuseaux synchronés bilatéraux. Le trait indique la duré d'une stimulation olfactive qui provoque un arousal.
D. 1 heure après destruction du ganglion de Gasser gauche: synchronisation généralisée. La flèche indique le moment de la pénétration d'une électrode dans la substance réticulée et le début de la réaction d'éveil provoquée qui durera 2 min.

fréquence réduite''. Pour élucider les raisons d'une telle contradiction nous nous sommes placés dans des conditions expérimentales aussi proches que possible de celles de cet auteur. Pour ce faire, un enregistrement électrocorticographique des régions frontale, temporale et occipitale d'un hémisphère a été effectué. Mais pour être en mesure de juger des modifications globales de l'activité électrique corticale, et pas seulement de celles survenant sur les aires de projection spécifiques, l'activité des régions homologues de l'autre hémisphère était enregistrée simultanément en électroencéphalographie.

Quatre expériences de section des nerfs optiques et trois de section de nerfs acoustiques nous ont permis d'observer, sur les aires réceptrices correspondantes mises à nu, l'apparition de bouffées d'ondes lentes à 7-10 c/sec. (fig. 6). Les résultats de Claes sont donc confirmés, bien que dans nos expériences ces activités synchronisées étaient séparées par des périodes de rythmes rapides de normale amplitude. Nos données expérimentales ont d'autre part permis trois remarques: 1) les modifications EEG de l'aire spécifique, du fait de leur basse amplitude, sont surtout appréciables sur le cortex mis à nu (fig. 6, B); 2) les fuseaux focalisés sont généralement à cadence plus lente que ceux qui caractérisent un état de sommeil; 3) la tendance à la synchronisation de l'aire spécifique désafférentée est surtout visible quand le ''background'' généralisé de sommeil est aboli (fig. 6, C).

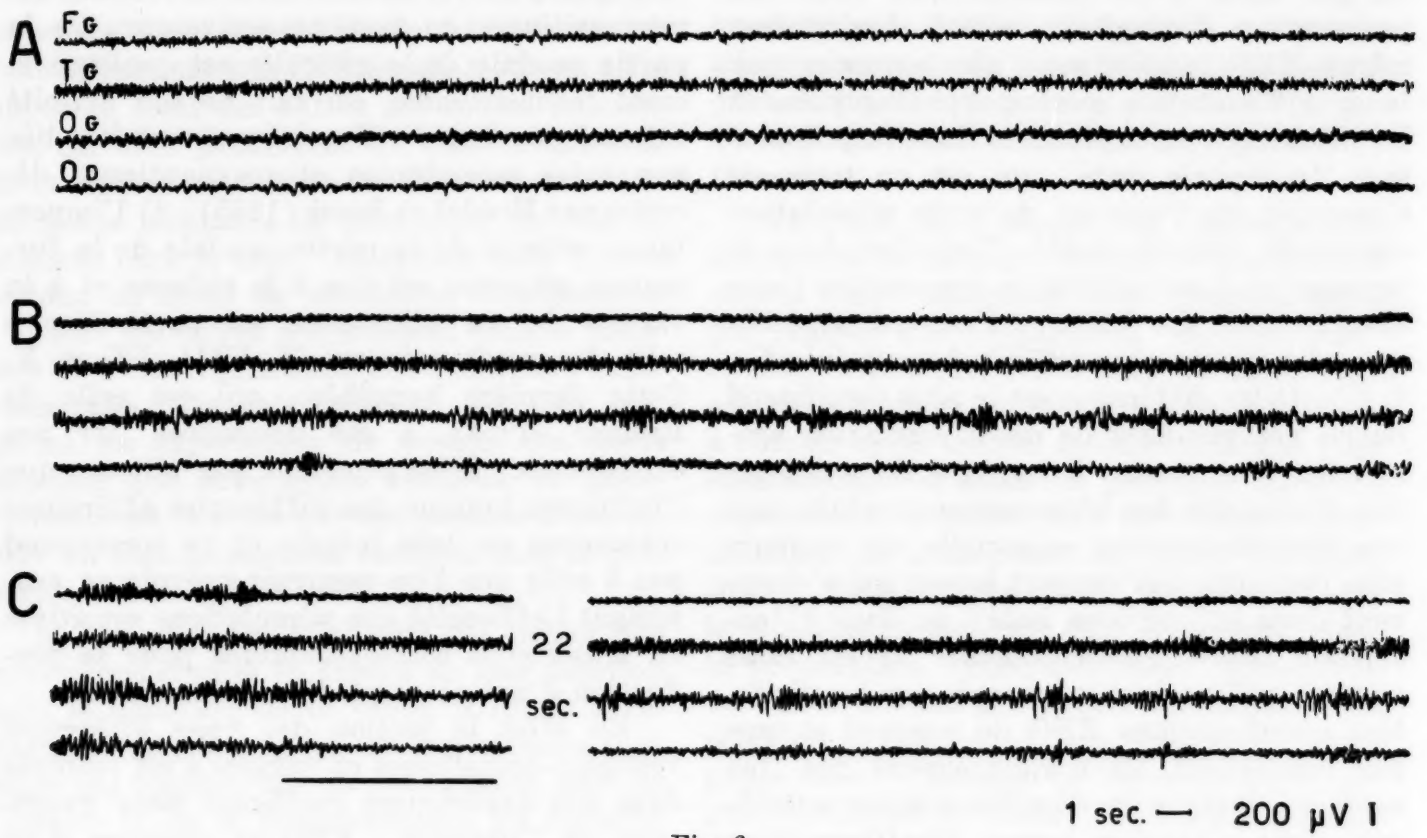

Fig. 6

Effet de l'interruption des voies optiques sur l'activité de l'aire réceptrice primaire. (Les 3 premières dérivations correspondent à l'enregistrement électrocorticographique.)

A. ½ heure après section rétrobulbaire du névraxe: activation généralisée.

B. 1 heure après section des nerfs optiques: tracé activé sur les régions frontale et temporale: présence de fuseaux d'ondes lentes localisés aux régions occipitales. Remarquer la différence existant entre les activités recueillies en électrocorticographie et en électroencéphalographie.

C. 1 heure 30 min. après section des nerfs optiques: tracé de sommeil. Le trait indique la durée de la stimulation auditive (sifflet). Noter la réapparition prématurée des fuseaux synchronisés sur l'aire occipitale mise à nu.

La première de ces observations explique la divergence apparente entre les données de Claes et nos résultats EEG.

Les observations suivantes peuvent contribuer à mettre en évidence les différences considérables existant entre ces synchronisations focalisées et le syndrome EEG de sommeil qui s'observe après interruption du système réticulaire ascendant (''cerveau isolé'') ou par effet d'une gasserectomie chez une préparation ''encéphale isolé''. Les phénomènes EEG induits sur l'aire primaire par la désafférentation sont morphologiquement les mêmes que ceux observés dans la préparation ''encéphale isolé'' qui est en train de s'assoupir, en l'absence de toute stimulation sensorielle intentionnelle. Toutefois dans le premier cas il est possible de reconnaître l'aire désafférentée du fait que l'arousal aspécifique est toujours plus difficile à produire (fig. 6, C). Cette différence est le plus significatif parmi nos résultats de désafférentation sensorielle. Par contre il importe de souligner que l'intensité des phénomènes produits par une désafférentation sensorielle est toujours plus restreinte par rapport à ceux qui s'observent dans le ''cerveau isolé'' ou dans l'''encéphale isolé'' gasserectomisé. Il est donc naturel qu'ils soient submergés par les véritables manifestations EEG de sommeil et que, par conséquent, ils n'apparaissent pas ''en surface'' lorsque la désafférentation spécifique vient s'ajouter à une désafférentation anatomique ou fonctionnelle, par rapport aux systèmes à projection diffuse.

DISCUSSION

Dans la préparation ''cerveau isolé'', obtenue par une section mésencéphalique ou pontine post-trigéminale, la portion rostrale de la formation réticulée restant en connexion avec le cortex n'est pas suffisante au maintien de la veille, malgré l'apport des impulsions des voies olfactives et visuelles. L'inefficacité hypnogène de la suppression des influx parcourant ces systèmes sensorielles a été confirmée dans nos expériences pratiquées chez le chat ''encéphale isolé''. C'est donc à la substance réticulée bulbaire et pontine que revient une importance critique dans le maintien de la veille, chez la préparation ''encéphale isolé''.

Trois hypothèses peuvent être envisagées pour expliquer ces résultats: 1) la partie caudale du système réticulé ascendant ne diffère pas, au moins du point de vue qualitatif et fonctionnel, des parties rostrales du même système, le sommeil du ''cerveau isolé'' étant tout simplement la conséquence de la réduction quantitative, au-dessous d'un certain niveau critique, du système activateur; 2) la partie caudale de la réticulée est qualitativement insubstituable, du fait de son activité intrinsèque, dont l'efficacité pourrait être liée aux voies ascendantes olygosynaptiques décrites par Brodal et Rossi (1955); 3) l'importance critique de la partie caudale de la formation réticulée est due à la richesse et à la variété de ses afférences, en particulier à celle des nerfs crâniens V, VIII, IX et X. Cette dernière hypothèse, qui est celle de Bremer (1954), a été démontrée par nos expériences. Elles prouvent par ailleurs que l'influence tonique des différentes afférences crâniennes est très inégale et ne correspond pas à celle que l'on pourrait prévoir en examinant l'efficacité des stimulations sensitives ou sensorielles correspondantes pour la production d'une réaction d'éveil transitoire.

En effet la section des voies afférentes vestibulo-acoustiques et vagales s'est montrée dans nos expériences inefficace pour provoquer les ''patterns'' EEG et cliniques d'un état de sommeil chez le chat ''encéphale isolé'' Cependant l'excitation de ces mêmes voies provoque aisément une activation globale transitoire des rythmes cérébraux et une réaction d'éveil lorsque l'animal dort. Selon nos données les systèmes vestibulo-acoustique et vagal se comportent donc, en ce qui concerne le maintien ''tonique'' de l'état vigile, comme les voies olfactives et visuelles.

Par contre, confirmant les données préliminaires de Rossi et Zirondoli (1955), nos recherches ont montré le rôle critique de la section des voies trigéminales pour le passage de l'état de veille à celui de sommeil. Des expériences de contrôle ont établi que l'apparition des manifestations EEG et du syndrome clinique du sommeil consécutive à la

destruction de ganglions de Gasser, était effectivement liée à la suppression des influx afférents trigéminaux.

L'interruption par voie extracrânienne de la IXème paire n'ayant pû être réalisée, nous ne sommes pas en mesure de discuter l'apport éventuel de la suppression des afférences glosso-pharyngiennes dans le mécanisme du sommeil. Il ressort des expériences de Bonvallet, Dell et Hiebel (1954) que les décharges issues du sinus carotidien, dont la voie centripète appartient à la IXème paire, ont un effet opposé à celui des autres afférences crâniennes, car elles produisent un état de sommeil. Si la section globale de la IXème paire était au moins incapable de provoquer un état de sommeil chez le chat ''encéphale isolé'', nous serions en droit de considérer fondamental l'apport des influx trigéminaux dans le maintien de l'état vigile dans nos conditions expérimentales. Jusqu'à présent, en tout cas, parmi les expériences de section des nerfs crâniens que nous ayons réalisées, la gasserectomie est la seule qui soit capable d'engendrer un état de sommeil continu, chez la préparation ''encéphale isolé''.

Si l'on envisage la variété des influx que nous avons étudiés en regard de leur fonction dans le maintien de la veille, il serait à remarquer que les impulsions trigéminales sont celles qui transportent la plus grande part de l'extéro- et de la proprioception du segment céphalique, tandis que les nerfs vagues transmettent des influx viscéraux et que les nerfs VIII, II et I sont des voies sensorielles. La position du nerf glosso-pharyngien, que nous n'avons pas étudié, est intermédiaire, car il transmet à la fois des impulsions sensitives et viscérales (sinus et glomus carotidien). Un animal ''encéphale isolé'', dont l'ensemble du système réticulé est en continuité avec le télencéphale, mais dont les voies de la sensibilité profonde et superficielle du tronc et membres est interrompue, présente un état fonctionnel labile à la limite de la veille et du sommeil. Cette donnée permet de suggérer que le sommeil engendré dans cette préparation par la section des voies trigéminales, résulte d'une plus complète suppression des modalités de la sensibilité extéro-, proprio- et nociceptive.

La distribution généralisée des spindles apparaissant après la section uni- ou bilatérale des voies trigéminales laisse supposer que la modalité d'action de la déconnection trigéminale est aspécifique. C'est là une différence importante par rapport aux manifestations EEG localisées qui suivent l'interruption d'une voie sensorielle. Il est donc très vraisemblable que les effets de la gasserectomie et ceux de la désafférentation optique qui ont été décrits pour la première fois par Claes (1939), obéissent à des mécanismes différents.

Au cours de l'exposé des résultats nous avons noté la moindre fréquence des spindles chez le chat ''encéphale isolé'' gasserectomisé par rapport à la préparation ''cerveau isolé'' et nous avons fait remarquer qu'un arousal olfactif (Arduini et Moruzzi 1953), difficile à obtenir après section mésencéphalique, était constamment et aisément provoqué dans nos expériences. D'autre part les données préliminaires de recherches en cours (Mollica, Roger, Rossi et Zirondoli) démontrent que la stimulation corticale peut provoquer, dans la préparation ''encéphale isolé'' gasserectomisée, un arousal généralisé. On sait que cet effet est présent dans la préparation ''encéphale isolé'' (Bremer et Terzuolo 1954; Segundo, Naquet et Buser 1955), mais manque dans le ''cerveau isolé'' (Mollica 1955). Ces constatations suggèrent que les parties caudales de la substance réticulée sont déprimées par la suppression des afférences toniques trigéminales mais peuvent encore être ébranlées par des volées corticifuges et olfactives.

L'interprétation de nos données serait en somme la suivante: l'état vigile est la conséquence d'une activité réticulaire entretenue par des décharges centripètes toniques, dont le caractère serait surtout extéro- et proprioceptif. L'importance des afférences sensorielles et viscérales dans les mécanismes toniques liés au maintien de l'état vigile apparaît peu considérable. L'activité automatique du système réticulaire ascendant, si elle existe, ne paraît pas suffisante pour main-

tenir un état vigile chez la préparation ''encéphale isolé''.

RÉSUMÉ

Pour tenter d'élucider la part revenant aux impulsions hétérogènes convergents sur le système réticulé ascendant, et plus généralement aux afférences sensitivo-sensorielles, dans le maintien de l'état vigile, des expériences consistant en la désafférentation de certains nerfs crâniens ont été effectuées chez le chat ''encéphale isolé'', par conséquent privé des modalités sensibles extéro- et proprioceptives du tronc et des membres.

1. La section des voies olfactives, optiques, acoustico-vestibulaires et vagales, n'a pas entraîné de modifications frappantes dans l'état fonctionnel plus ou moins vigile du chat ''encéphale isolé''.

2. Le rôle critique de la section des voies trigéminales pour le passage de l'état de veille à celui de sommeil a été démontré par des expériences de gasserectomie.

3. Des expériences de contrôles ont établi que l'apparition des manifestations EEG et du syndrome clinique du sommeil, consécutives à la destruction des ganglions de Gasser chez la préparation ''encéphale isolé'', était effectivement liée à la suppression des influx trigéminaux centripètes.

4. Des expériences chroniques ont permis de confirmer toutes les données recueillies dans les préparations aiguës.

5. Des expériences ont précisé les données de Claes à propos des modifications EEG focalisées sur l'aire de projection spécifique consécutives à la suppression d'une modalité sensorielle.

6. L'ensemble des faits expérimentaux mis en évidence tend à faire admettre que l'état vigile serait la conséquence d'une activité de la substance réticulaire entretenue par des impulsions de caractère essentiellement extéro- et proprioceptif, plutôt que d'une activité intrinsèque de cette formation du tronc de l'encéphale. Le rôle tonique des afférences sensorielles et viscérales paraît beaucoup plus réduit.

SUMMARY

With the aim of studying the role of various sensory modalities in the maintenance of wakefulness, different cranial nerves have been severed in ''encéphale isolé'' cats.

1. No definite modification of the EEG pattern of alertness characteristic of the ''encéphale isolé'' preparation has been produced by suppressing olfactory, visual, acoustic, vestibular or vagal afferents.

2. The waking EEG pattern of the ''encéphale isolé'' cat has been changed into one of sleep by bilateral destruction of the Gasserian ganglion.

3. That this phenomenon is really a consequence of suppression of trigeminal centripetal influences has been demonstrated in control experiments.

4. These findings have been confirmed in chronic preparations.

5. Previous observations (Claes 1939) concerning EEG changes localized to cortical sensory areas, following section of the specific projecting nerves, have been confirmed and discussed.

6. The evidence derived from the present experiments suggests that the waking state might be the consequence of a reticular activity maintained by extero- and proprioceptive impulses rather than intrinsic in origin. The tonic role of the other sensory modalities is probably much less important.

BIBLIOGRAPHIE

AMASSIAN, V. E. Organisation in somatosensory systems. *Fed. Proc.*, **1952**, *11*: 5.

AMASSIAN, V. E. and DEVITO, R. Unit activity in reticular formation and nearby structures. *J. Neurophysiol.*, **1954**, *17*: 575-603.

ARDUINI, A. and MORUZZI, G. Olfactory arousal reactions in the ''cerveau isolé'' cat. *EEG Clin. Neurophysiol.*, **1951**, *3*: 189-196.

BAUMGARTEN, R. VON and MOLLICA, A. Der Einfluss sensibler Reizung auf die Entladungsfrequenz kleinhirnabhängiger Reticularzellen. *Pflügers Arch.*, **1954**, *259*: 56-78.

BONVALLET, M., DELL, P. et HIEBEL, G. Tonus sympatique et activité électrique corticale. *EEG Clin. Neurophysiol.*, **1954**, *6*: 119-144.

BREMER, F. ''Cerveau isolé'' et physiologie du sommeil. *C. R. Soc. Biol.*, Paris, **1935**, *118*: 1235-1242.

BREMER, F. Nouvelles recherches sur le mécanisme du sommeil. *C. R. Soc. Biol.*, Paris, **1936**, *122*: 460-464.

BREMER, F. Activité électrique du cortex cérébral dans les états de sommeil et de veille chez le chat. *C. R. Soc. Biol.*, Paris, **1936**, *122*: 464-467.

BREMER, F. The neurophysiological problem of sleep. In *Brain Mechanism and Consciousness*, Oxford, Blackwell, **1954**.

BREMER, F. et TERZUOLO, C. Contribution à l'étude des mécanismes physiologiques du maintien de l'activité vigile du cerveau. Interaction de la formation réticulée et de l'écorce cérébrale dans le processus du réveil. *Arch. int. Physiol.*, **1954**, *62*: 157-178.

BRODAL, A. and ROSSI, G. F. Ascending fibers in brain stem reticular formation of cat. *Arch. Neurol. Psychiat.*, Chicago, **1955**, *44*: 68-87.

CHOROBSKI, J. and PENFIELD, W. Cerebral vasodilator nerves and their pathway from the medulla oblongata. *Arch. Neurol. Psychiat.*, Chicago, **1932**, *28*: 1257-1289.

CLAES, E. Contribution à l'étude physiologique de la fonction visuelle. I. Analyse oscillographique de l'activité spontanée et sensorielle de l'aire visuelle corticale chez le chat non anesthésié. *Arch. int. Physiol.*, **1939**, *48*: 181-237.

COBB, S. and FINESINGER, J. E. Cerebral circulation. XIX. The vagal pathway of the vasodilator impulses. *Arch. Neurol. Psychiat.*, Chicago, **1932**, *28*: 1243-1256.

DARROW, C. W., GREEN, J. R., DAVIS, E. W. and GARXOL, H. W. Parasympathetic regulation of high potentials in the electroencephalogram. *J. Neurophysiol.*, **1944**, *7*: 217-226.

FORBES, H. S., NASON, G. I., COBB, S. and WORTMAN, R. C. Cerebral circulation. XLV. Vasodilation in the pia following stimulation of the geniculate ganglion. *Arch. Neurol. Psychiat.*, Chicago, **1937**, *37*: 776-781.

LEGAIT, E. Corpuscules nerveux dans la paroi des artères du réseau admirable carotidien. *C. R. Soc. Biol.*, Paris, **1945**, *139*: 340-341.

LINDSLEY, D. B., BOWDEN, J. and MAGOUN, H. W. Effect upon the EEG of acute injury to the brain stem activating system. *EEG Clin. Neurophysiol.*, **1949**, *1*: 475-486.

LINDSLEY, D. B., SCHREINER, L. H., KNOWLES, W. B. and MAGOUN, H. W. Behavioral and EEG changes following chronic brain stem lesions in the cat. *EEG Clin. Neurophysiol.*, **1950**, *2*: 483-498.

MOLLICA, A. Assenza di reazione elettroencefalografica di risveglio nel gatto "cerveau isolé" per stimolazioni elettriche corticali. *Boll. Soc. it. Biol. sper.*, **1955**, *31*: 249-250.

MORUZZI, G. and MAGOUN, H. W. Brain stem reticular formation and activation of the EEG. *EEG Clin. Neurophysiol.*, **1949**, *1*: 455-473.

PENFIELD, W. and MCNAUGHTON, F. Dura headhache and innervation of the dura mater. *Arch. Neurol. Psychiat.*, Chicago, **1940**, *44*: 43-75.

ROSSI, G. F. and ZIRONDOLI, A. Sulle strutture anatomiche che permettono la veglia nel gatto "encefalo isolato". *Boll. Soc. it. Biol. sper.*, **1954**, *30*: 494-495.

ROSSI, G. F. and ZIRONDOLI, A. On the mechanism of the cortical desynchronization elicited by volatile anesthetics. *EEG Clin. Neurophysiol.*, **1955**, *7*: 383-390.

SCHEIBEL, M., SCHEIBEL, A., MOLLICA, A. and MORUZZI, G. Patterns of convergence and interaction of afferent impulses on single units on the reticular formation. *J. Neurophysiol.*, **1955**, *18*: 309-331.

SEGUNDO, J. P., NAQUET, R. and BUSER, P. Effects of cortical stimulation on electrocortical activity in monkeys. *J. Neurophysiol.*, **1955**, *18*: 236-245.

Reference: ROGER, A., ROSSI, G. F. et ZIRONDOLI, A. Le rôle des afférences des nerfs crâniens dans le maintien de l'état vigile de la préparation "encéphale isolé". *EEG Clin. Neurophysiol.*, **1956**, *8*: 1-13.

PRINTED IN CANADA

ANNOUNCEMENT

The XIIth National Congress of The Italian Neurological Society will be held at Padova, April 4-7, 1956.

Subjects to be covered are the following:

(1) Modern trends in the subject of the encephalitides (C. Berlucchi, V. Longo).

(2) Problems in epilepsy: (*a*) pathogenesis of the epileptic attack (M. Gozzano;); (*b*) epilepsy and the vegetative nervous system (O. Malecci); (*c*) medical treatment of epilepsy (S. Rigotti).

Communications should be limited to the above-mentioned subjects; decision regarding other outstanding contributions not related to them is reserved to the President of the Organization Committee. Sufficient time will be allotted for extensive discussion of each paper.

Authors are requested to submit a typed manuscript together with a summary of not more than ten lines for publication in the Programme, to:

The Organization Committee
Clinica Neuropsichiatrica
Padova, Italy

before the end of February 1956.

Members of the Congress will find accommodation at Abano, where the sessions following the inaugural plenary one are to take place. Further instructions regarding the mode of reservation for accommodation shall be sent to members of the Congress.

Prof. G. B. BELLONI, *President of the Organization Committee.*

Prof. V. M. BUSCAINO, *President of The Italian Neurological Society.*

EFFECT OF MESCALINE AND L.S.D. ON EVOKED RESPONSES ESPECIALLY OF THE OPTIC SYSTEM OF THE CAT [1]

PIERO ROVETTA, M.D.
Institute of Neurophysiology, University of Copenhagen, Denmark

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In 1898, Heffter reported his own experiences after ingestion of four different Peyotl alcaloids (Anhalonium Lewinii). He established that the previously described subjective disturbances evoked by this drug were due to mescaline (for references, see Heffter 1898; Beringer 1927; and Morselli 1950). These disturbances are recently vividly described in "The doors of perception" (Huxley 1954) and involve most spectacularly the visual system. Colors take on a new vividness, there are optical illusions and hallucinations with moving and colored patterns. More complex psychic alterations involve the sense of time and of reality, and initiative. Somatic disorders include nausea, vertigo, mydriasis, slowing of the pulse and ataxia (Heffter 1898; Dixon 1899). Changes in the EEG are confined to a decrease in amplitude (Walter 1938; Davis 1942).

In animals, reports deal mainly with autonomic dysfunction (Heffter 1898; Raymond-Hamet 1932; Grace 1934; Clerc, Paris and Janot 1936). In addition, somnolence and ataxia (Heffter 1898; Dixon 1899), catatonic states and convulsions (De Jong 1930) have been described. Hart and Marrazzi (1952, 1953, 1955) reported a diminution in the amplitude of cortical responses evoked by contralateral cortical stimulation after intravenous mescaline. It seemed, therefore, of interest to study the effect of mescaline systematically and topically applied on responses evoked by light stimuli. The findings were confirmed for other sensory systems and for direct cortical stimulation. In view of certain similarities between mescaline and lysergic acid diethylamid (L.S.D.) (Stoll 1947; Matefi 1952) on psychosensory phenomena, the effect of intravenous and local L.S.D. was studied.

[1] Aided by a grant from the National Multiple Sclerosis Foundation of America and from the Danish State Research Foundation.

MATERIAL AND METHODS

The experiments were performed on 21 cats anesthetized with intramuscular chloralose-urethane (1 and 3.5 per cent respectively) at a usual initial dose of 8 cc. per kg. Additional anesthesia was given as necessary to reduce spontaneous electrical activity. The head was fixed in a Horseley-Clarke headholder. The pupil was kept widely dilated with 2 per cent atropine sulphate solution and the body temperature was regulated.

Operative procedure and electrode placement. The cortex was exposed with appropriate hemostasis. For recording of visual responses, the electrode was usually placed on the mid portion of gyrus lateralis, sometimes as well in posterior and anterior placements, and occasionally on posterior gyrus suprasylvius. For recording of responses to sciatic and acoustic stimuli, the electrodes were placed on gyrus sigmoideus posterior and gyrus ectosylvius respectively, at the point of maximum response.

In 7 cats the lateral geniculate body was exposed through gyrus ectosylvius and hippocampus, care being taken not to damage gyrus suprasylvius and lateralis. The electrode was placed in the body of the geniculate usually through its supero-lateral aspect.

The retinal electrode was placed on the postero-lateral surface of the eye ball, at the point of maximum response, after resection of the masticatory and lateral extraoccular muscles.

Recording technique. Cerebral responses were recorded with concentric needle electrodes containing a platinum core with a

recording area of 0.1 square mm. The recording depth was usually 0.5-0.8 mm., rarely 1.5-3 mm. Leading off took place between the core and the small area of the cannula (outer diameter 0.6 mm.) in contact with the tissue. The sign of the recorded potential depends on the position of the electrode relative to the activated cells and cannot be directly compared with unipolar recording. In the present measurements, maximal response amplitude was searched for independent of the sign. The electroretinogram was recorded with a silver placque, 3 mm. in diameter, and the reference electrode was placed on the stump of the ipsilateral temporal muscle. The animal was grounded at the headholder.

The amplifier was a 4 channel differentially coupled A-C amplifier with cathode follower input circuit and an input impedance of 100 megohms shunted by 60 $\mu\ \mu$ F. The lower limiting frequency was 1 c/sec., the upper limiting frequency 7000 c/sec. defined by 3 db. discrimination. The smallest measurable responses were approximately 10-20 μV. Single sweep responses were photographed on 35 mm. film from the screen of a double beam Dumont oscilloscope (type 279) at an appropriate sweep speed between 10 cm. to 3 m/sec. The sweep was triggered 1-2 msec. before onset of the sensory stimuli. The beginning and the end of each light flash or of electric or acoustic stimuli, led from the square wave generator, served as signal marking.

The light stimulation technique was very similar to that described (Lennox and Madsen 1955; Madsen and Lennox 1955). The light source was a Sylvania glow modulator tube (R 1130 B 2 white light). The light beam was focussed by two lenses at the cat's cornea where the light spot was 3 mm. in diameter. The color of the light could be altered by three interference filters each with a 20 mμ pass band and a maximum transmission at 445, 515 and 578 mμ. A fourth glass filter cut out light below 620 m μ.[1] The maximum intensity of white light was 754 μW. per square cm.; of green light 11,8 μW. per cm^2; of blue light 8.6 μW. per cm^2; of yellow light 79 μW. per cm^2; and of red light 638 μW. per cm^2. The intensity could be decreased by neutral filters in 12 steps over a 5 decade range. Threshold for white light could only be reached by diminishing the pulse width. It was approximately 0.002 μW. per square cm. with a 10 msec. flash. The rectangular light stimulus had a rising time of 0.8 msec. and a total duration of 33 msec., occasionally 2 or 10 msec. The stimulus frequency was one in 2 sec. Stimulation was carried out with the eye in complete darkness and after an initial 20 min. period of dark adaption.

Acoustic stimulation consisted of clicks at an intensity of five times the threshold of a just measurable cortical response. Sciatic stimulation was carried out between 2 electrodes placed across the sciatic nerve; direct cortical stimulation between two 0.1 mm. platinum wires, 0.5 mm. apart, placed in light contact with the cortex. Electrical stimuli consisted of single rectangular current pulses applied via a double-screened transformer (Buchthal, Guld and Rosenfalck 1955).

Substances. Mescaline chloride[2] was applied topically (filter paper) as a 5, 9, 20 and 33 per cent solution (by weight) in saline. The intravenous dose was 7 to 15 mg. per kg. *Strychnine sulphate* was applied topically as a 0.5 or 3.5 per cent solution in saline. *Lysergic acid diethylamid* (L.S.D. 25) was applied topically in a 0.001, 1, 5 and 9 per cent solution in saline and intravenously at a dosage of 20 to 40 μg. per kg.

Measurement of potentials. Each response was recorded 5 to 10 times, and the values for amplitude and latency represent a mean of these 5 to 10 measurements.

The *amplitude* of the *cortical potentials* was measured from the base line to the peak of the first deflection and from the maximum negative to the maximum positive peak.

Geniculate response amplitude was measured from the base line to the peak of the first positive, and from the peak of the first positive to the peak of the following negative deflection.

Amplitude of the *retinal potentials* was measured from the base line or from the peak

[1] The author is indebted to Dr. Bent Buchmann-Olsen, Department of Biophysics, and Annelise Madsen, E.E., Institute of Neurophysiology, who performed the calibration of the light source, neutral and color filters (to be published).

[2] Mescaline was kindly supplied by Medicinalco, Copenhagen, and L. S. D. by Sandoz, Basel.

of the first positive to the peak of the following negative deflection.

Latency was measured for *cortical* potentials as the time interval between the onset of the light stimulus and the first departure from the base line. The *geniculate latency* was measured to the onset of the first positive deflection; *retinal latency* to the onset of the positive deflection.

plane. With increasing depth (above 0.5 mm.), the second phase of the potential tended to be more prominent (fig. 1 A_1, A_2). The peak to peak amplitude increased with increasing light intensity up to 400 μV. The latency varied between 18 msec. at maximum to 65 msec. at weak illumination.

The first effect of mescaline could be observed 1 to 5 min. after local application

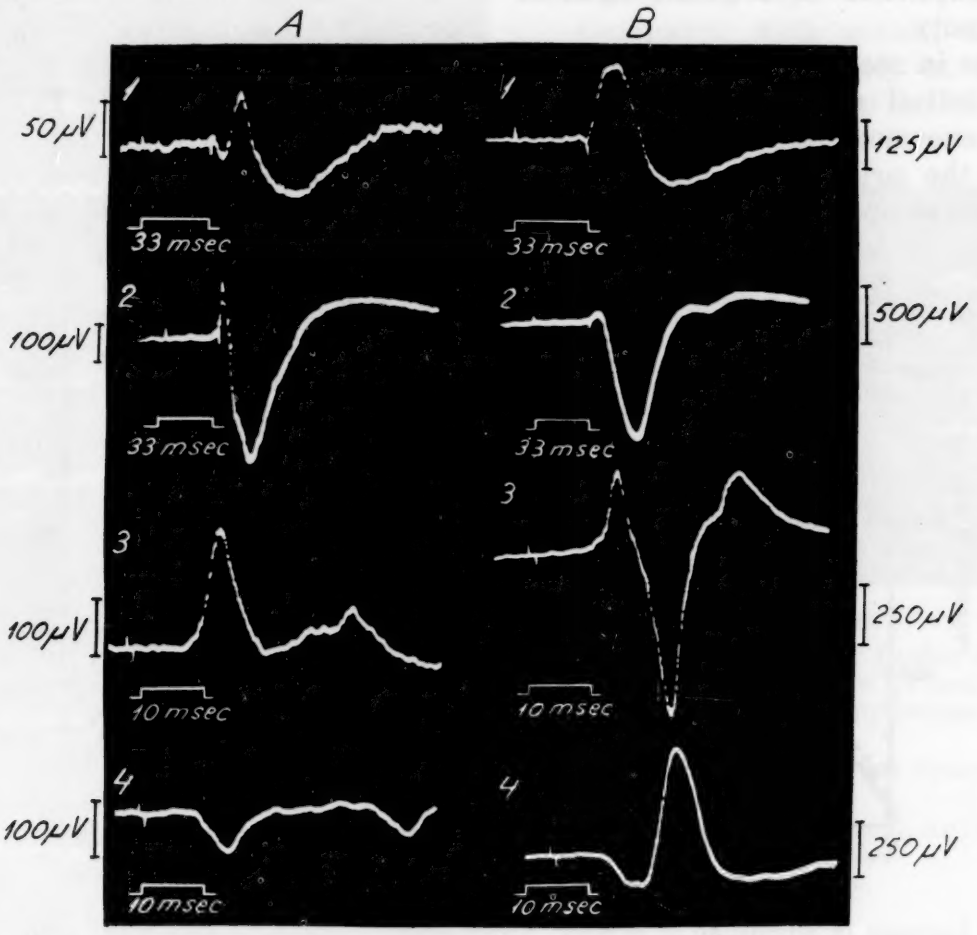

Fig. 1

Examples of cortical responses to white light flashes, intensity 67 μW. per cm^2. Column A before and column B after local application of 33 per cent mescaline. Flash duration 1 and 2, 33 msec.; 3 and 4, 1 msec. Time after application of mescaline 1, 7 min.; 2, 30 min., 3 and 4, 15 min.
Needle location 1, 2 and 3 mid portion gyrus lateralis, 1 and 2 at depth 1 mm, 3 at 0.5 mm; 4 posterior gyrus lateralis at 1 mm depth.
Upward deflection negative.

RESULTS

1. MESCALINE:

Effect of topically applied mescaline on evoked responses from optic cortex.

"On" response in untreated cortex. Four examples of responses evoked by white light stimuli are given in figure 1 A, corresponding essentially to the description by Marshall, Talbot and Ades (1943). There was no clear relationship between type of response and electrode placement in the anterior-posterior

(fig. 1 B). For a period of 20 to 45 min., the *response amplitude* increased progressively and then stayed at its maximum for 15 to 60 min. (fig. 2 and 3). When the filter paper with mescaline was removed after 15 min., the pre-mescaline values were reached within 2 hours. The percentage increase in amplitude over the pre-mescaline value tended to be higher with the highest mescaline concentrations. During the mescaline effect, a change in stimulus intensity had no effect on the

response amplitude. Even threshold stimuli evoked responses of the same amplitude as did stimuli of maximum intensity (fig. 4). At threshold, a response might not appear to each stimulus, but whenever a potential did appear it was of maximum amplitude. This obtained irrespective of the color of the flash. A threshold red light evoked a response of the same amplitude as a green light of maximum intensity.

The increase in response amplitude, up to 30 times the initial amplitude, was attributable to an enormous increase in a later component of the primary response. Sometimes this second component was visible in the pre-mescaline response (fig. 1 A_1, A_2). When the second component could not be distinguished in the pre-mescaline response, it was evoked by application of the drug (fig. 1 B_3 and B_4, fig. 3). The first phase of the response was usually increased about twofold in the early stages of mescalinization; later it might even be decreased in amplitude.

The *latency* of cortical responses increased with increasing time of mescaline action, up to 20 per cent one hour after application of the drug. The latency of the second phase of the response was disproportionately increased so that the time interval between the first and the second phase was greater after than before mescaline (fig. 1, 3, 4).

The amplitude of the off-response might be increased somewhat in early mescalinization; when the mescaline effect was fully developed, the "off" was lost in the large mescaline spike (fig. 4 A).

Acoustic and sciatic stimulation did not evoke responses in mescalinized optic cortex, nor did light stimuli evoke responses in mescalinized cortex outside electrophysiologically defined areas (Marshall, Talbot and Ades, 1943).

The degree and time course of the amplitude and latency increase was the same as at primary optic cortex when mescaline was applied to gyrus suprasylvius posterior.

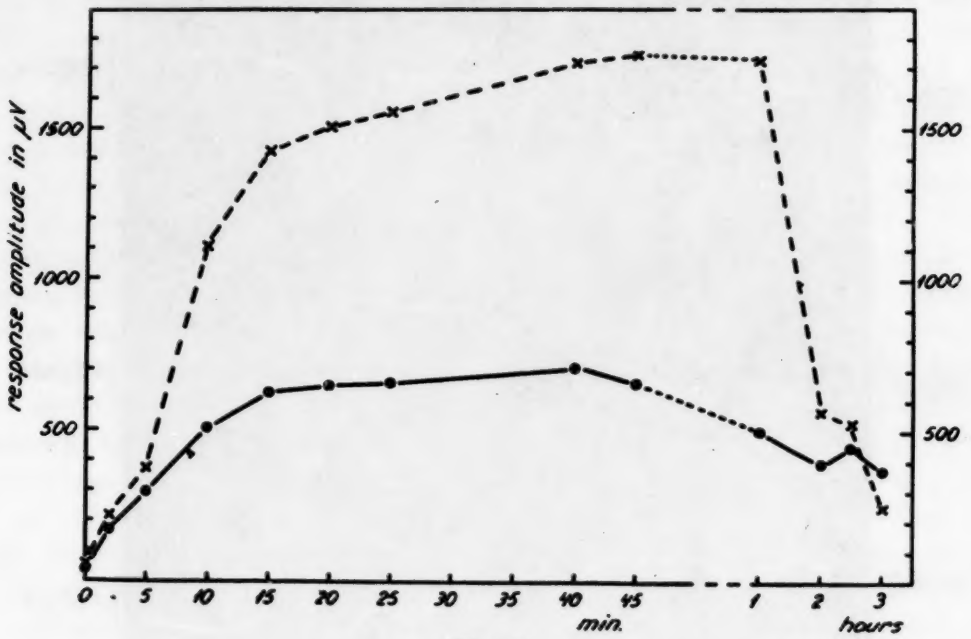

Fig. 2

Increase in amplitude of cortical responses to white light flashes 33 msec. duration, intensity 21 μW. per square cm as a function of time during local application of 33 per cent mescaline (cat 35).
x ·—— x total amplitude
●——● initial negative amplitude

Effect of topically applied mescaline on lateral geniculate responses evoked by light stimuli.

Before mescaline the main geniculate "on" response was positive and was frequently double (fig. 5 A), the second positive deflection varying somewhat in amplitude and position with light intensity and from cat to cat, but becoming increasingly prominent with increasing light intensity. At the highest intensities a third positive deflection was fre-

quently seen (fig. 5, 3). A negative phase of lower amplitude followed this positive complex; especially at high intensities an initial negative wave might be seen. The whole response was superimposed by small fast spike discharges with a maximum amplitude of 25-35 μV. and at intervals of 1-2 msec. characteristic for the spontaneous activity of the lateral geniculate (Dubner and Gerard 1939).

The maximum total amplitude of the evoked geniculate response was up to 200 μV.; the amplitude of the first positive phase up to 160 μV. The latency of the first positive phase was 15-20 msec. with stimuli of high intensity and 50-60 msec. with stimuli near threshold intensity.

Compared with cortex, mescaline acted considerably more slowly on the lateral geniculate, probably due to the fact that the drug had to diffuse through the encasing fibre layer. An enhancement of all components of the evoked response was observed 15 min. after application of a 20-33 per cent solution of the drug (fig. 5 C). A maximum enhancement of four times the original value was seen one hour after application of the drug.

The latency of the geniculate responses remained unaltered by mescaline.

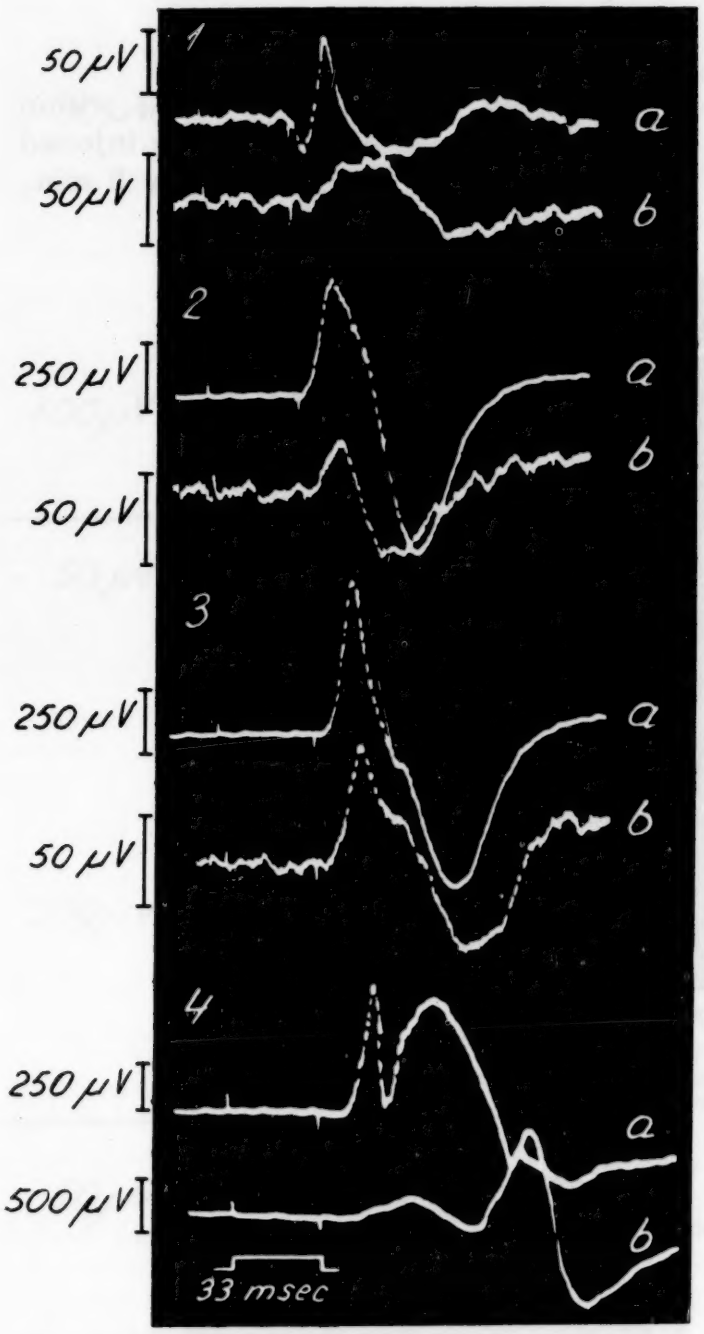

Fig. 3

Responses to light flash from gyrus lateralis (a) and posterior suprasylvian gyrus (b) before and at various time intervals during local 33 per cent mescaline at electrode (a). 1, before mescaline; 2, 25 min. after mescaline; 3, 35 min. after mescaline; 4, 120 min. after mescaline. Light flash white, intensity 220 μW. per square cm, duration 33 msec. Upward deflection negative.

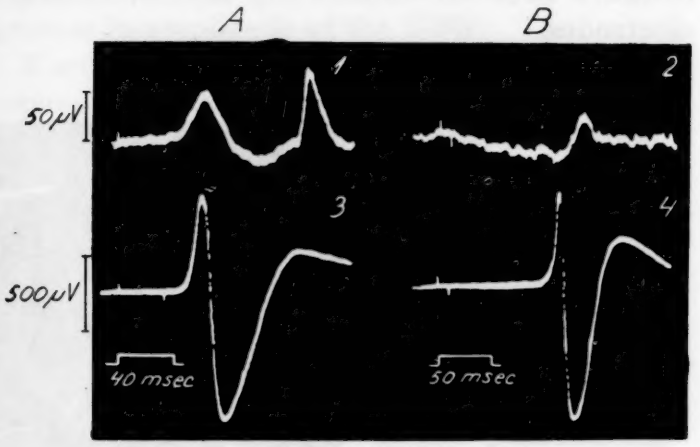

Fig. 4

Cortical responses to light flashes of large (A) and small (B) intensity before (1 and 2) and 30 min. after (3 and 4) local application of 33 per cent mescaline.

A. Light intensity 67 μW. per square cm, flash duration 33 msec.

B. Light intensity at threshold, 0.0124 μW. per square cm, flash duration 10 msec.

Upward deflection negative.

Other sensory systems.

As with light stimulation, local mescaline applied to somato-sensory cortex (fig. 6, $_{1a, b,}$ gyrus sigmoideus posterior) and acoustic cortex (fig. 6, $_{2a, b,}$ gyrus ectosylvius posterior) caused an up to 20 fold increase in amplitude of a second component of the response while the first component only in-

creased two to threefold. The latency showed no significant change.

As with light stimulation, the off-response to click was at first slightly increased and under full mescalinization was lost in the large mescaline spike.

Direct electrical stimulation of visual cortex.

In the untreated cortex, a response of simple wave form was evoked (fig. 6, 3a), surface positive and with increasing latency and decreasing amplitude according to the distance between stimulating and recording electrodes.

Action of mescaline on spontaneous cortical activity.

One hour after topical application large spontaneous spikes (up to 2 mV.) or potentials with two or more phases occurred simultaneously on 2 electrodes in mescalinized cortex resembling very much spontaneous strychnine spikes.

Effect of intravenous mescaline.

Autonomic effects. During and within the first 15 min. after intravenously injected mescaline at a rate of 10 mg. every 2 min.,

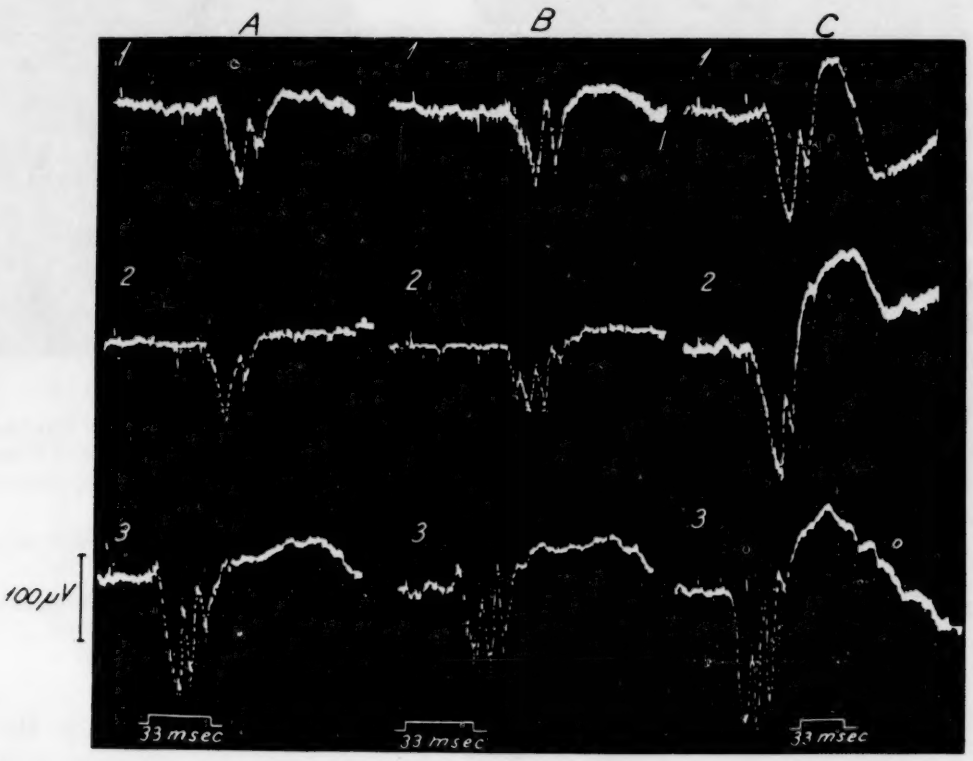

Fig. 5

Responses from lateral geniculate to white light flash before (A), after intravenous (B) and after local mescaline (C) at different light intensities. 1, 1.3 μW. per square cm; 2, 7.2 μW. per square cm; 3, 740 μW. per square cm; flash duration 33 msec.

B. 1, 5 min.; 2, 15 min.; 3, 30 min. after intravenous 9 mg. per kg. mescaline.

C. 20 min. after 20 per cent local mescaline.
Upward deflection negative.

The effect of mescaline applied between the stimulating and the recording electrode is illustrated in fig. 6 3b. As with light stimulation, a high amplitude second component of the response appeared, and the latency of the first component was prolonged. Electrical excitability was *decreased* so that threshold was increased 2 to 3 times after mescaline.

defecation, urination and piloerection occurred regularly. The cardiac rhythm was irregular with periods of slow and of increased rate. Similarly there were periods of apnoea. These disturbances usually disappeared within 10 to 15 min.; one animal died, however, from respiratory failure immediately after injection of 27.7 mg. per kg.

Effect on potentials evoked in the visual system by light stimuli.

Retinal potentials. Before intravenous mescaline, the retinal potential had a main surface negative deflection, i.e. opposite in direction to the retinogram as recorded between an electrode on the cornea and a distant indifferent electrode (Granit 1955, p. 153). In 9 of 11 cats, the amplitude increased by an average of 20 per cent. The latency showed slight decreases rarely exceeding 10 per cent. It cannot be ruled out that the changes were due to more complete dark adaption.

Lateral geniculate. Immediately after mescaline the amplitude of the evoked responses was slightly diminished (not exceeding 20 per cent), but the different components of the response were somewhat more clearly distinguishable than before (fig. 5 B). The decrease in amplitude obtained in spite of the increase in amplitude of the ERG.

Cortical responses. The cortical evoked responses showed a diminution (15-20 per cent) in both positive and total amplitude (fig. 7). This diminution fluctuated irregularly between 0 and 20 per cent during the 2 hour observation period after drug administration. When slight latency changes occurred they were in the direction of a decrease by no more than 10 per cent. The amplitudes and latencies of responses to the four color stimuli relative to the retinal amplitude were

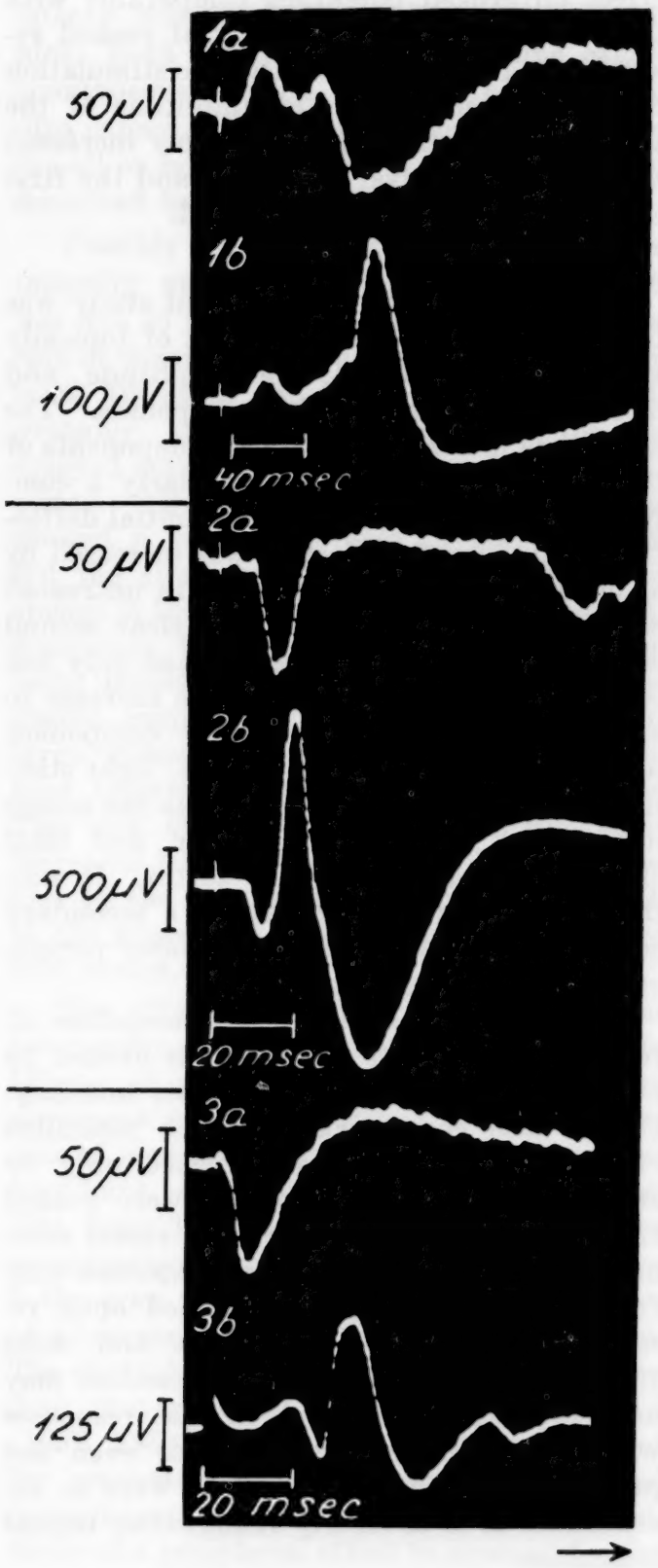

Fig. 6

Cortical responses evoked by sciatic (1a, b), acoustic (2a, b), and direct electrical (3a, b) stimulation. Before (a) and after (b) topically applied 20 per cent mescaline.

1a, b: sciatic stimulation, three times threshold, pulse duration 0.5 msec. 1b, time after mescaline 2 hours.

2a, b: click stimulus, five times threshold, 2b, time after mescaline 5 min.

3a, b: response recorded 2 mm from direct cortical stimulation. Stimulus intensity about threshold, pulse duration 0.5 msec. (a), 1 msec. (b). 3b, time after mescaline 1 hour.

Upward deflection negative.

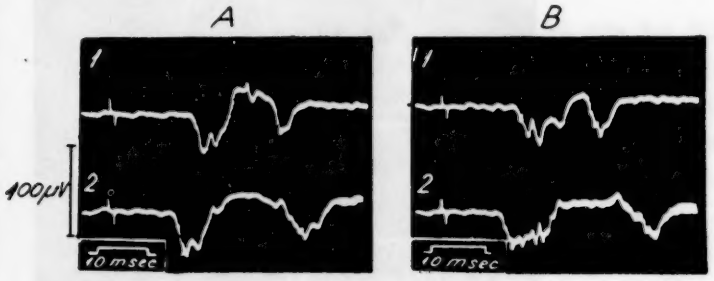

Fig. 7

Responses from optic cortex to white light flashes before (A) and after (B) intravenous mescaline, 12.5 mg. per kg.

Light intensity: 1, 7.2 μW per square cm; 2, 67 μW. per square cm; flash duration, 1 msec. Amplitude of electroretinogram: 1A, 130 μV.; 1B, 140 μV.; 2A, 354 μV.; 2B, 408 μV.

the same after as before intravenous mescaline both at cortex and at geniculate.

2. TOPICALLY APPLIED STRYCHNINE:

The cortical potentials evoked by visual stimuli after application of mescaline appeared qualitatively similar to the effect of strychnine (fig. 8).

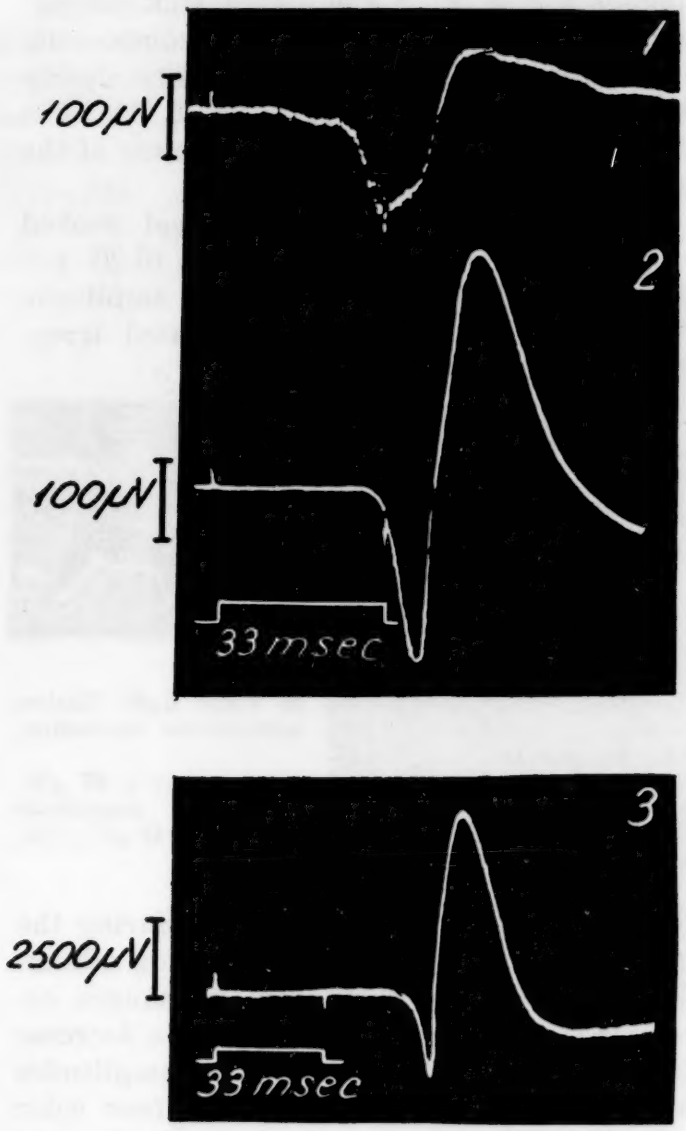

Fig. 8

Response from optic cortex to light flash before (1), and at 5 (2) and 20 min. (3) after local 3.5 per cent strychnine sulphate. White light, intensity 21 μW. per square cm, flash duration 33 msec. Upward deflection negative.

Both mescaline and strychnine caused an enhancement especially of the second component of the response, an increase in latency and in spontaneous spikes. The effects of strychnine were, however, more pronounced in that the amplitude of the evoked response was greater and the full effect developed more quickly. As with mescaline, the strychnine response was "all or none" not only for white but also for colored light.

3. LYSERGIC ACID DIETHYLAMID (L.S.D.):

Topical L.S.D. even in such large concentrations as 9 per cent and intravenous L.S.D. in dosages up to 40 μg. per kg., had no effect on evoked potentials comparable with that of mescaline. The latency of evoked responses to light flash and acoustic stimulation remained unchanged. The amplitude of the second component was questionably increased and the time interval between it and the first component was slightly prolonged.

DISCUSSION

The main result of the present study was the finding of the marked effect of topically applied mescaline on the amplitude and latency of evoked cortical responses. The amplitude increase involved all components of the response, but most spectacularly a component which occurred after the initial deflection. This second deflection was increased by as much as thirty time its value in untreated cortex, and might appear as a clear second component in a response which had only one component before mescaline. The increase in amplitude of a second response component occurred with all types of stimuli: light stimulus to the eye, electric stimulus to the sciatic nerve, click stimulus to the ear, and local electrical stimulation of the cortex. It was, therefore, due to an increase in a secondary central event, rather than in a later peripherally released discharge.

It was characteristic of the mescaline effect that a maximal response was evoked by every stimulus no matter what its intensity. It was also characteristic of the mescaline effect that responses were evoked only by adequate stimuli: no responses were evoked from visual cortex by other than visual stimuli, and visual stimuli evoked responses only from electrophysiologically defined optic receiving areas (Marshall, Talbot and Ades 1943). This characteristic of mescaline may have practical application, in that responses which were either very small or even not present before topical mescaline were so accentuated as to be clearly visible after topical mescaline.

In the present study, the effect of topical strychnine on evoked cortical responses was qualitatively identical to that of mescaline; quantitatively, the effect of strychnine was greater than with mescaline. The strychnine effect was the same as that described by Bishop and Clare (1952) with the exception that in the present experiments the response latency was markedly prolonged by strychnine. Both strychnine and mescaline caused spontaneous spiking. The fact that any stimulus caused a maximum response is very like the all or none evokation of strychnine spikes described by Chang (1951-1953).

Possibly the different effect of mescaline topically applied to the lateral geniculate was due to the different effective concentration of the drug. Diffusion through the overlying fibres to the body of the geniculate probably accounted in any case for the delayed action of the drug as compared with cortex. All phases of the primary response showed a modest increase in amplitude, as did the first component of the cortical response in the initial phases of drug action. At geniculate, there was not the clear cut enormous increase in amplitude of a later response component. In one cat there were large spikes, but they occurred at various time intervals after the primary response. The lack of an essentially and constantly increased later component may be an expression of the relative paucity of internuncials in the geniculate (Glees 1941) as compared with cortex.

The effects of locally applied mescaline are puzzling. In the case of strychnine, the effects of the drug applied topically are consonant with the systemic effects. In the case of mescaline, this was not so. Mescaline may have convulsant action in some species (De Jong 1930), but its main effect is the accentuation of visual sensation. Puzzling too is the very minor effect on evoked responses of intravenous mescaline, even in large doses. The slight decrease in amplitude was even less than that reported by Hart and Marrazzi (1952, 1953, 1955), and the appearance of the responses in many instances suggested desynchronization. Nor was there clear evidence of a peripheral effect to account for the enhancement of visual impressions reported clinically.

Finally, the autonomic changes observed in this study after intravenous mescaline are similar to those described by Heffter (1898), Dixon (1899), Raymond-Hamet (1932), Grace (1934), Clerc *et al.* (1936). It seems at least possible that these autonomic effects may account in part at least for the central effects of intravenous mescaline.

The lack of an effect with topical and intravenous lysergic acid diethylamid is in contrast with the findings of Marrazzi and Hart (1955) and with the clinical experience (Stoll, 1947) that L.S.D. is effective in much smaller doses than mescaline.

SUMMARY

Mescaline chloride (in solutions up to 33 per cent by weight) was applied topically to the cortex and lateral geniculate of the cat and its effect on evoked responses was studied. Responses were evoked by local cortical stimulation and from appropriate sensory receiving areas by flash stimuli to the eye, both of white and of four colors; click to the ear; and electrical stimulation to the sciatic nerve.

With all types of stimuli mescaline had the same marked effect on amplitude and latency of evoked cortical potentials. The effect appeared within 5 min., reached its maximum at about 30 min. and declined after 2 to 4 hours. The *amplitude* was increased up to 30 times and this was attributable to an increase in the amplitude of a second component of the response. The first component increased two- to threefold or might even be slightly decreased. The maximal response was obtained with stimuli of all intensities and in the visual system with light of all colors. The *latency* was prolonged to light flash and to direct cortical stimulation. The latency to sciatic and to acoustic stimulation was not changed.

Responses were evoked only by adequate stimuli; no responses were evoked from visual cortex by other than visual stimuli, and visual stimuli evoked responses only from known optic receiving areas.

When the cortical effect was fully develop-

ed, large (2 mV.) spontaneous spikes appeared.

At lateral geniculate, mescaline produced a two- to fourfold increase in all components of the response to light flash. Latency was not altered.

Local strychnine (3.5 per cent) produced qualitatively the same effect as mescaline on evoked responses to light flash but the effect was more marked in that the amplitude of the response was greater and the full effect developed more quickly. In other respects — increase in latency, increase in amplitude of a second component of the response, "all or none" response to every stimulus and evokation of spontaneous spikes — strychnine and mescaline acted identically on evoked responses to light flash.

Intravenous mescaline in doses up to 15 mg. per kg. produced immediate, temporary autonomic changes consisting of cardiac irregularity, periods of apnoea, piloerection, urination and defecation. There was a slight decrease in the amplitude and increase in the duration of cortical and geniculate potentials evoked by light flash.

Topical and intravenous lysergic acid diethylamid (up to 9 per cent solution by weight, or 40 μg. per kg.) produced no clear cut effect comparable to that of mescaline on evoked response amplitude. The time interval between the first and second components of the cortical response was prolonged.

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REFERENCES

BERINGER, K. *Der Meskalinrausch.* J. Springer, Berlin, **1927.**

BISHOP, G. H. and CLARE, M. H. Sites of origin of electric potentials in striate cortex. *J. Neurophysiol.*, **1952**, *15*: 201-220.

BUCHTHAL, F., GULD, C. and ROSENFALCK, P. Propagation velocity over electrically activated muscle fibres in man. *Acta physiol., scand.*, **1955**, *34*: 75-89.

CHANG, H. T. An observation on the effect of strychnine on local cortical potentials. *J. Neurophysiol.*, **1951**, *14*: 23-28.

CHANG, H. T. Similarity in action between curare and strychnine on cortical neurones. *J. Neurophysiol.*, **1953**, *16*: 221-233.

CLERC, A. R., PARIS, R. et JANOT, M.-M. Contribution à l'étude expérimentale du sulphate de mescaline. *C. R. Soc. Biol.*, Paris, **1936**, *121*: 1300-1302.

DAVIS, P. A. Comparative study of the EEGs of schizophrenic and manic-depressive patients. *Amer. J. Psychiat.*, **1942**, *99*: 210-217.

DE JONG, H. Ueber Meskalin-Katatonie und die experimentelle Erzeugung von Dementia praecox-Erscheinungen. *Kong. Akad. Wetenschap.* Amsterdam (Section Sci.), **1930**, *33*: 1076-1081.

DIXON, W. E. The physiological action of the alkaloids derived from Anhalonium Lewinii. *J. Physiol.*, **1899**, *25*: 69-86.

DUBNER, H. H. and GERARD, R. W. Factors controlling brain potentials in the cat. *J. Neurophysiol.*, **1939**, *2*: 142-152.

GLEES, P. The termination of optic fibers in the lateral geniculate body of the cat. *J. Anat.*, **1941**, *75*: 434-440.

GRACE, G. S. The action of mescaline and some related compounds. *J. Pharmacol.*, **1934**, *50*: 359-372.

GRANIT, R. *Receptors and Sensory Perception.* Yale University Press, New Haven, **1955**, pp. 366.

HART, E. R. and MARRAZZI, A. S. Cerebral synaptic action of mescaline. *J. Pharmacol.*, **1952**, *106*: 349.

HEFFTER, A. Ueber Pellote. *Arch. exp. Path. Pharmak.*, **1898**, *40*: 385-429.

HUXLEY, A. *The Doors of Perception.* Chatto & Windus, London, **1954**, pp. 63.

LENNOX, M. A. and MADSEN, A. Cortical responses to colored light flash in the cat. *J. Neurophysiol.*, **1955**, *18*: 412-424.

MADSEN, A. and LENNOX, M. A. Responses to colored light flash from different areas of optic cortex and from retina in the anesthetized cat. *J. Neurophysiol.*, **1955**, in press.

MARRAZZI, A. S. and HART, E. R. Comparison of the effect on evoked cortical synaptic response of mescaline, amphetamine and adrenaline. *EEG Clin. Neurophysiol.*, **1953**, *5*: 317-318.

MARAZZI, A. S. and HART, E. R. Relationship of hallucinogens to adrenergic cerebral neurohumors. *Science*, **1955**, *121*: 365-367.

MARSHALL, W. H., TALBOT, S. A. and ADES, H. W. Cortical response of the anesthetized cat to gross photic and electrical afferent stimulation. *J. Neurophysiol.*, **1943**, *6*: 1-15.

MATEFI, L. Mescalin und Lysergsäurediäthylamid Rausch. *Confin. neurol.*, **1952**, *12*: 146-177.

MORSELLI, G. E. Recherches expérimentales et délires. *C. R. Congrès Intern. Psychiat.*, Hermann, Paris, **1950**, *1*: 89-121.

RAYMOND-HAMET. Neue Beobachtungen über die physiologische Wirkung des Mescalin. *Arch. exp. Path. u. Pharmakol.*, **1932**, *169*: 97-113.

STOLL, W. A. Lysergsäure-diäthylamid, ein Phantastikum aus der Mutterkorn-gruppe. *Schweiz. Arch. Neurol. Psychiat.*, **1947**, *60*: 279-303.

WALTER, W. G. The technique and application of electro-encephalography. *J. Neurol. Psychiat.*, **1938**, *1*: 359-385.

Reference: ROVETTA, PIERO. Effects of mescaline and L.S.D. on evoked responses especially of the optic system of the cat. *EEG Clin. Neurophysiol.*, **1956**, *8*: 15-24.

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MODIFICATIONS ÉLECTRO-ENCÉPHALOGRAPHIQUES, ÉLECTRO-DERMOGRAPHIQUES ET ÉLECTRO-MYOGRAPHIQUES PROVOQUÉES PAR LA CHLORPROMAZINE CHEZ L'HOMME

M. Turner, E. Bérard, N. Turner et N. Franco
Laboratorio de Electroneurofisiología Clínica, Buenos Aires, Argentina

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GÉNÉRALITÉS

L'introduction des techniques de neurolyse et les résultats cliniques obtenus en pratique psychiatrique ont motivé diverses recherches tendant à éclaircir le mécanisme d'action de la chlorpromazine (4560RP).

Récemment Hiebel, Bonvallet et Dell (1954) ont publié les résultats de leurs intéressantes expériences effectuées sur des animaux avec des méthodes électro-physiologiques qui ont permis de démontrer et d'analyser le lieu d'action et les mécanismes centraux intéressés. La chlorpromazine déprime l'activité des formations réticulées du tronc cérébral (Système d'activation réticulaire ascendant de Moruzzi et Magoun) dont dépend l'activité du cortex, en diminuant la sensibilité de ce système aux afférences sensorielles et noci-ceptives. En même temps elle inhibe les réactions activatrices adrénergico-sympathiques sur ces formations centrales devant les agressions les plus diverses.

La description des modifications électro-encéphalographiques observées chez l'homme a été envisagée par d'autres auteurs (Terzian 1952, 1954; Castro et Bérard 1954; Turner et Bérard 1954) qui ont conclu à la possibilité d'un mécanisme d'action analogue.

Au contraire des publications cliniques antérieures, et indépendamment des observations expérimentales, nous avons cru intéressant d'employer chez l'homme des méthodes dynamiques d'"électro-encéphalographie fonctionnelle", en ayant recours à divers procédés d'activation, avant, pendant et après l'injection de la drogue. Simultanément nous avons jugé digne d'attention l'enregistrement des manifestations végétatives sympathiques, au moyen de la réponse électro-dermale, et accessoirement nous avons enregistré les changements notés sur le registre électro-myographique. Nous avons supposé qu'avec cette technique il serait plus facile d'obtenir de plus amples éléments de jugement sur l'action de la chlorpromazine au niveau du système nerveux central et sur les changements provoqués par les divers stimuli.

Nous considérons que les résultats réguliers et constants obtenus jusqu'à présent sont suffisamment significatifs pour nous permettre d'élaborer les premières conclusions à ce sujet.

MATÉRIEL ET MÉTHODE

Vingt sujets ont été examinés (9 névroses, 2 psychoses, 5 épilepsies psycho-motrices, 1 épilepsie petit-mal, 1 épilepsie végétative, 1 Parkinson post-encéphalitique, 1 tic généralisé, dont l'âge allait de 25 à 69 ans et dont 5 seulement étaient des hommes.

On a procédé à l'enregistrement électro-encéphalographique courant, premièrement en condition de repos psycho-physique, avec un appareil Kayser de 8 canaux. Simultanément on enregistrait l'électro-dermogramme au moyen de deux électrodes placées sur le dos et sur la paume de la main, branchées sur un canal de l'appareil utilisant une constante de temps de 0,6 sec. et une amplification adéquate (technique de Bloch et Paillard, 1951). Dans quatre cas nous avons enregistré l'électro-myogramme avec des électrodes superficielles. Nous avons employé les activations suivantes: hyperpnée, stimulation lumineuse intermittente, stimulation auditive (sons d'acuité et d'intensité variables), stimulation verbale, etc., stimuli noci-ceptifs et thermiques, et dans un cas le Cardiazol test (technique de Gastaut).

Puis nous avons procédé à l'injection lente intra-veineuse d'une solution contenant 50 mg. de chlorpromazine dans 20 cm³ de sérum physiologique. La dose de la drogue a oscillé entre 20 et 50 mg. L'enregistrement et les activations ont été répétés, à des intervalles réguliers jusqu'à 1 heure après l'injection de la drogue. La dose totale injectée dépendait de la réaction clinique et électrographique du malade, de façon que l'on suspendait l'injection dès l'apparition de modifications notoires dans un aspect ou dans l'autre. Pendant l'injection on faisait adopter au malade la position de décubitus dorsal et à la fin de l'expérience celui-ci devait se rasseoir très lentement.

Dans 5 cas nous avons injecté préalablement à l'injection de chlorpromazine 10 cm³ de sérum physiologique i.v. avec le même débit que l'injection de la drogue. Toutes les

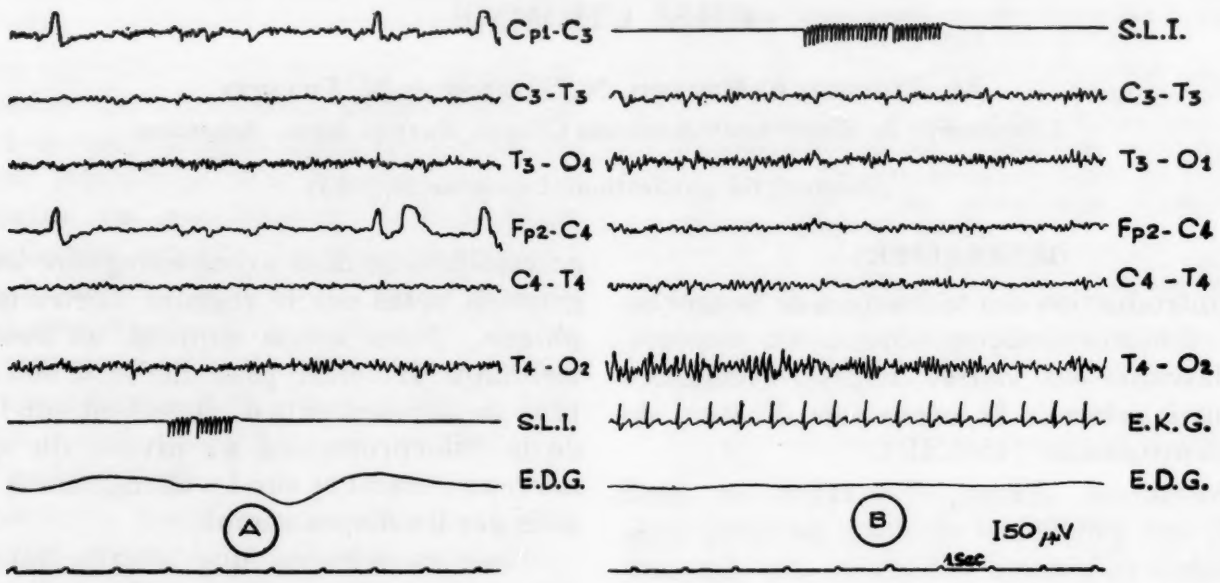

Fig. 1

Cas No 1081

Femme de 54 ans, neurotique.

A. *Avant chlopromazine.* Tracés du type hyperactif, désynchronisés, de faible amplitude et fréquences rapides. Le tracé électrodermographique (EDG) montre des oscillations provoquées par la stimulation lumineuse intermittente (SLI).

B. *Une demie heure après l'injection i.v. de 22 mgr. de chlorpromazine.* Synchronisation des tracés surtout dans la région occipitale droite: apparition d'un rythme alpha à 9-10 c/sec. de 50-150 μV. Stabilisation et absence de réponse de l'EDG.

(Pour raisons techniques on a branché la SLI sur le premier canal et on enregistre dans le septième l'électrocardiogramme: EKG.)

(Disposition d'électrodes dans ce cas et dans tous les autres cas d'accord au système « 10-20 »: Fp1, fronto-polaire gauche; C3, central gauche; T3, temporale moyenne gauche et O1, occipitale gauche; Fp2, C4, T4 et O2 positions comparables du côté droit.)

(L'échelle d'amplification —50 μV. est valable seulement pour les tracés EEG.)

Case No. 1081

54 years old woman, neurotic.

A. *Before chlorpromazine*: Activated pattern: desynchronised record of low amplitude with sporadic rapid frequencies. The electrodermographic record (EDG) shows the oscillations provoked by the flickering light (SLI).

B. *Half an hour after the i.v. injection of 22 mgr. of chlorpromazine.* Synchronisation of the EEG record, especially in the right occipital projection: appearance of an alpha rhythm of 9-10 c/sec. and 50-150 μV. Stabilization of the EDG. No response to the SLI.

(For technical reasons the photocell record in this figure appears in the 1st. channel. In the 7th. channel the electrocardiogram (EKG) is recorded.)

(In this and in the other cases the positions of ''10-20 electrode system'' are used: Fp1, frontal pole; C3, Central; T3, midtemporal; O1, Occipital on the left side; Fp2, C4 T4 and O2 are the comparable positions of the right side.)

(The amplification scale —50 μV. is applicable only to the EEG records.)

stimulations indiquées plus haut ont été réalisées par la suite. Tous les malades ignoraient la nature de la solution injectée.

RÉSULTATS OBTENUS

I. *Après l'injection de sérum physiologique*: aucune modification de la morphologie et de la réactivité des tracés n'a été observée.

II. *Après l'injection de 4560 R.P.*: entre 10 et 15 minutes après l'injection de la drogue, les modifications suivantes ont été observées:

a) *Observations électroencéphalographiques*: sur 5 tracés normaux nous avons observé, sur 3 d'entre eux, une très discrète diminution de la fréquence du rythme de fond (de 10 c/sec. à 8-9 c/sec.).

Sur 8 tracés d'aspect désynchronisé (faible amplitude, fréquences sporadiques rapides de 15 à 20 c/sec., blocus peu accentué à l'ouverture palpébrale, etc.) nous avons observé les modifications suivantes: 10 à 30 min. après l'injection on note une meilleure synchronisation (augmentation de l'amplitude et du pourcentage d'ondes alpha à fréquence normale).

Dans 5 cas, où nous avons observé des décharges d'irritation, de petites pointes, des ondes aiguës et lentes dans la région temporale, il y a eu une augmentation nette des décharges dans tous les cas et une irradiation vers la région temporale opposée dans 3 cas. Dans aucun des cas nous n'avons noté des manifestations de crise clinique.

Dans un cas avec tracé normal, où l'activation photocardiazolique a provoqué au bout du cinquième cm^3 (3 mg. par kg. de poids) une désynchronisation diffuse du tracé et de nombreuses oscillations électro-dermographiques, accompagnées cliniquement de myoclo-

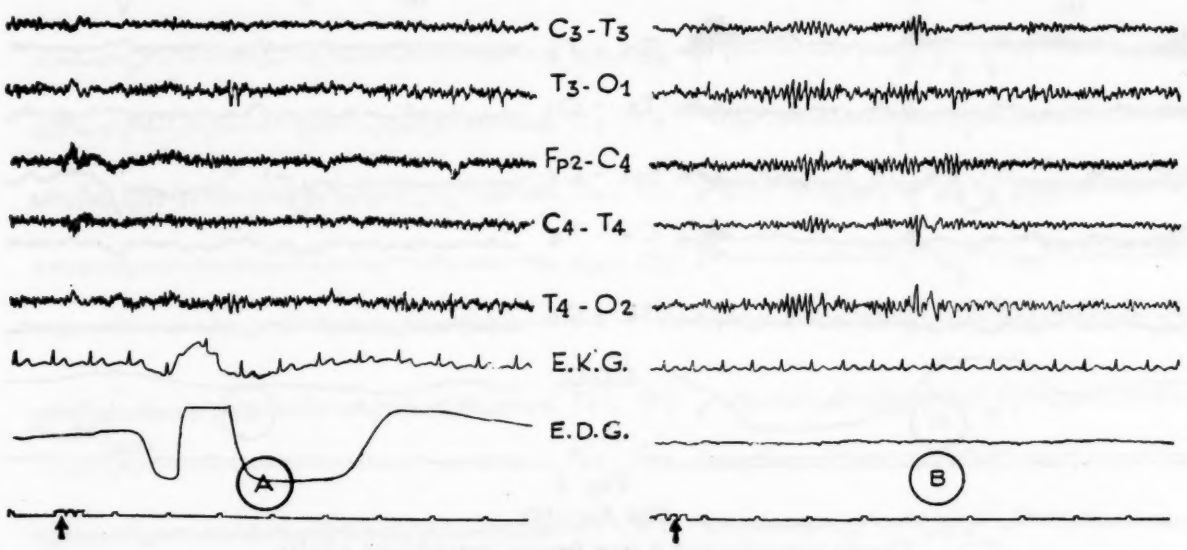

Fig. 2

Cas No 891

Malade de 58 ans, neurotique.

A. *Avant chlorpromazine.* Tracé EEG de type désynchronisés qui révèlent un état particulier d'hiperexcitabilité neuropsychique. Réponse électrodermographique (EDG) notable au stimulus nociceptif: piqûre avec une épingle.

B. *Une demie heure après l'injection i.v. de 30 mgr. de chlorpromazine.* Synchronisation des tracés EEG avec l'apparition des rythmes de fond à 8-9 et 10-11 c/sec. de plus grande amplitude. Disparition de la réponse électrodermographique même à un stimulus nociceptif.

Case No. 891

58 year old, neurotic patient.

A. *Before the administration of the chlorpromazine.* Desynchronized EEG records (activated pattern) indicating a state of nervous tension. Remarkable electrodermographic (EDG) response to a nociceptive stimulus (pin prick).

B. *Half an hour after the i.v. injection of 30 mgr. of chlorpromazine.* Synchronisation of the EEG record with the appearance of background rhythms at 8-9 and 10-11 c/sec. of greater amplitude. Disappearance of the EDG response to the nociceptive stimulus.

nies palpébrales, de transpiration abondante (enregistrée au moyen d'épreuves chromatiques) et accompagnées d'une sensation subjective désagréable de frissons et d'angoisse motrice avec état semi-confusionnel (crise semblable à celles dont le malade souffrait), l'injection de chlorpromazine a provoqué la disparition des troubles, le tracé reprenant au bout de 10 min. un aspect similaire au tracé antérieur à l'activation, avec abolition presque complète de la réponse électro-dermale aux divers stimuli. Dans 1 cas de petit mal avec des décharges de pointes-ondes à 3 c/sec. la chlorpromazine a déterminé une activation nette du tracé, les décharges devenant plus rapprochées et d'une plus longue durée.

b) *Observations électro-dermographiques*: dans tous les cas les oscillations de l'électrodermogramme répondant aux divers stimuli ont été très évidentes. Chez les sujets névrosés nous avons observé de fréquentes oscillations spontanées sans stimulus extérieur apparent. L'injection de chlorpromazine a déterminé dans tous les cas une stabilisation de la ligne de base avec disparition complète ou presque complète des réponses à tous les stimuli, y compris les noci-ceptifs.

c) *Observations électro-myographiques*: l'activité électro-myographique a été appréciée dans quelques cas sous formes d'extériorisations électro-myographiques aux électrodes temporales. Nous l'avons observée fré-

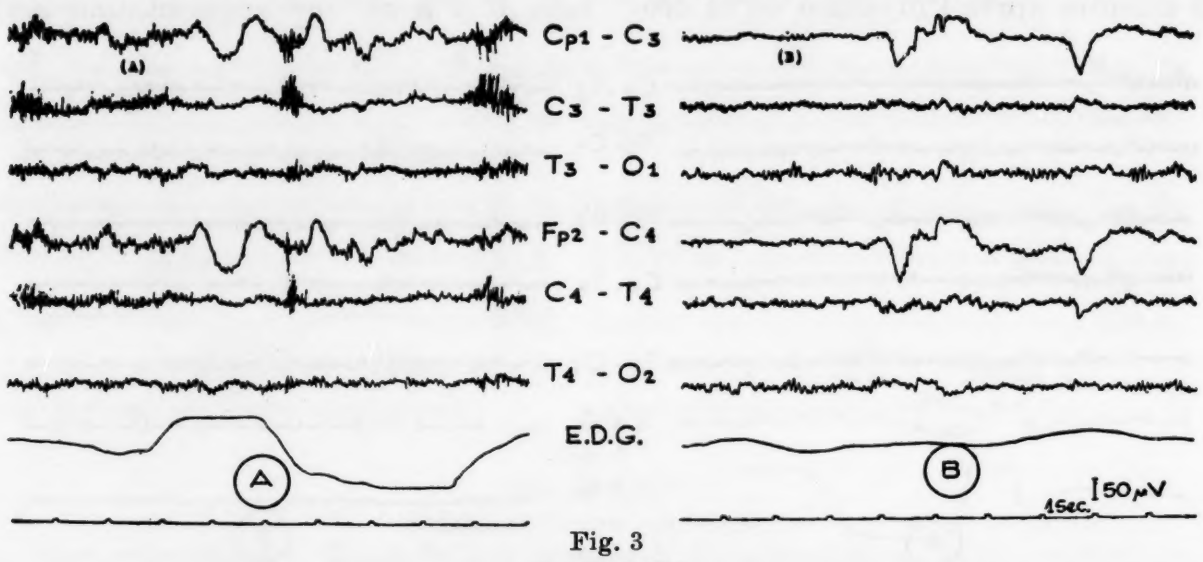

Fig. 3

Cas No 1136

Tracés appartenant à une femme neurotique adulte.

A. *Avant l'injection de chlorpromazine.* Tracés EEG caractérisés par leur aspect désynchronisé — faible amplitude, absence d'un rythme de fond stable et présence de fréquences sporadiques rapides de 15-20 c/sec. — très marqué d'artifices électromyographiques, conséquence de l'état de tension neuropsychique de la malade. Electrodermogramme (EDG) caractérisé par de fréquentes oscillations spontanées et provoquées par des stimuli divers.

B. *Une demie heure après l'injection i.v. de 25 mgr. de chlorpromazine.* On observe une meilleure synchronisation des tracés EEG avec apparition d'un rythme alpha à 10 c/sec. dans les régions occipitales. Diminution des artifices électromyographiques et stabilisation de la curve électrodermographique.

Case No. 1136

EEG records of an adult neurotic woman.

A. *Before chlorpromazine.* Activated and desynchronised pattern — low amplitude and sporadic rapid frequencies 15-20 c/sec. — masked by the electromyographic potentials exaggerated by the patient's state of nervous tension. The electrodermographic record (EDG) is characterized by oscillations. Some of them spontaneous, others provoked by different stimuli.

B. *Half an hour after the i.v. injection of chlorpromazine.* There is better synchronisation of the EEG records with appearance of an alpha rhythm of 10 c/sec. in the occipital regions and great diminution of the electromyographic artifacts and a stabilization of the EDG.

quemment chez les sujets névrosés à tension intra-psychique augmentée, s'exagérant pendant les différentes stimulations. Dans un cas de maladie de Parkinson post-encéphalitique avec tremblement de la moitié du corps, les extériorisations du tremblement (6 c/sec.) masquaient le tracé électro-encéphalographique correspondant et le EMG enregistré avec une électrode superficielle placée sur le masséter du même côté.

mettant ainsi un enregistrement électro-encéphalographique correct.

d) *Observations cliniques*: les malades deviennent plus calmes, plus tranquilles, indifférents à l'examen, les stimuli qui auparavant les faisaient sursauter et réagir d'une façon exagérée (réaction non modifiée après l'injection de sérum physiologique), ne paraissent pas les émouvoir après l'administration de chlorpromazine, (même les stimuli noci-

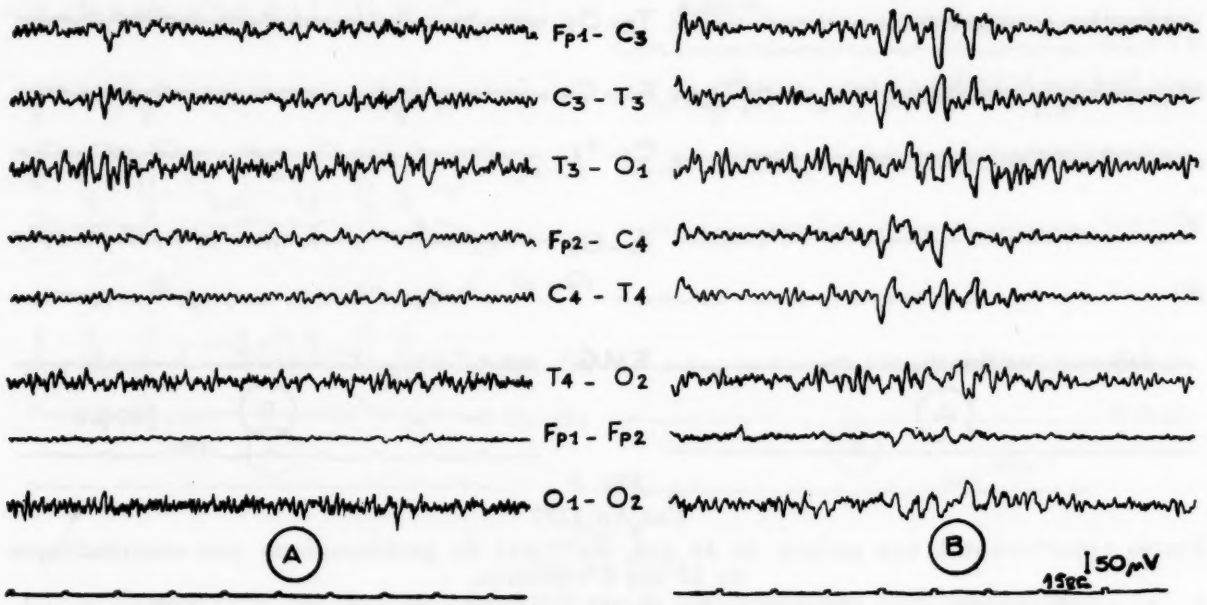

Fig. 4

Cas No 1151

E. R. Femme de 27 ans. Depuis 6 ans crises psychomotrices typiques.

A. *Réaction à l'hyperpnée avant chlorpromazine.* Pointes lentes sporadiques sur la région temporale gauche.

B. *Hyperpnée après injection de 30 mg. de chlorpromazine.* Décharges lentes (3-4 c/sec.) prédominant sur la région temporale gauche. Pas de crise clinique.

Case No. 1151

E. R. Woman, 27 years old. Typical psychomotor seizures for 6 years.

A. *Reaction to hyperventilation before intake of chlorpromazine.* Sporadic slow sharp waves over the left temporal region.

B. *Hyperventilation after injection of 30 mg. of chlorpromazine.* Slow (3-4 c/sec.) discharges predominating in the left temporal region. No clinical attack.

Dans le cas de « tics » généralisés chez une jeune fille de 21 ans, les mouvements involontaires ont été enregistrés comme artifices notamment sur les électrodes fronto-polaires et sur les tracés EMG par des électrodes placées sur les membres.

Dans ces deux cas l'injection de chlorpromazine a fait disparaître totalement ou presque totalement, dans la demi-heure qui a suivi l'injection, l'activité involontaire perceptifs) provoquant tout au plus une réaction légère. Malgré une certaine sensation de somnolence, en aucun moment les patients ne sombrent dans le sommeil et ils répondent facilement aux questions posées.

Les sensations subjectives ressenties par les malades sont par ordre de fréquence: somnolence, palpitations, vertiges, oppression thoracique, nausées. Ces symptômes ainsi que le contrôle de la tension artérielle et du

pouls ont servi d'indice pour interrompre l'administration de la drogue. La T.A. s'est abaissée de 1-4 cm de Hg. et le pouls a augmenté de 10 à 20 pour cent par rapport à la fréquence initiale. Les manifestations subjectives ont disparu peu de temps après la fin de l'injection. Parfois elles se présentaient au moment où le malade se levait, pour disparaître tout aussitôt dès qu'il s'allongeait à nouveau pendant quelques minutes (action hypotensive de la drogue). Cependant chez un sujet névrosé à l'extrême, les troubles subjectifs ont persisté pendant une période de 24 à 48 heures.

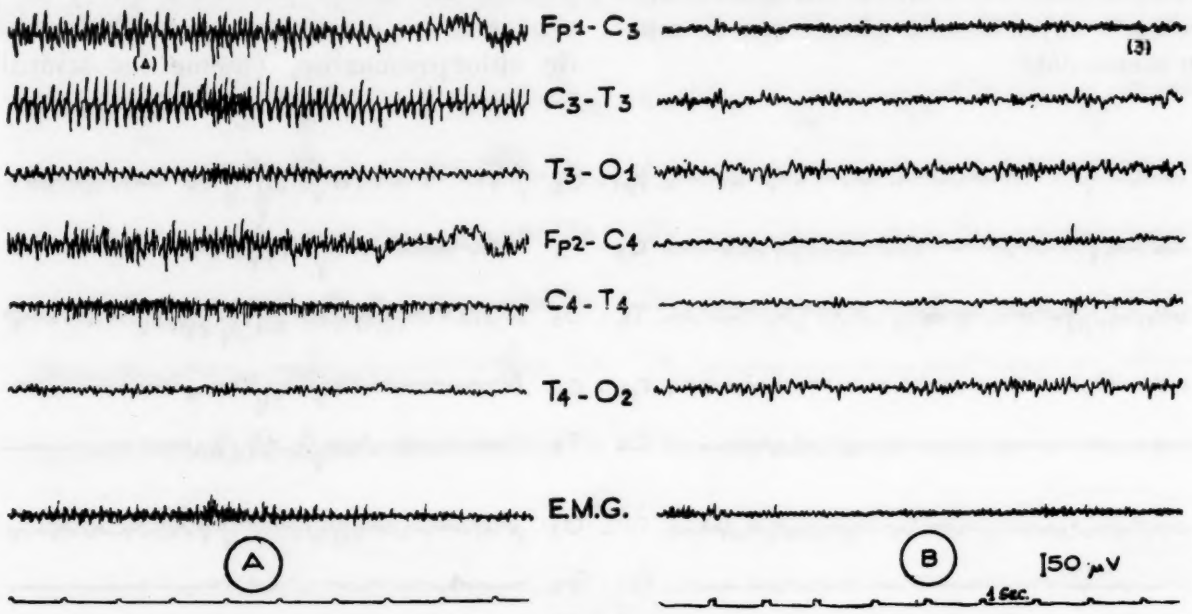

Fig. 5

Cas No 1137

Tracés appartenant à une malade de 44 ans, souffrant de parkinsonisme post-encéphalitique de 15 ans d'évolution.

A. *Avant chlorpromazine.* On observe les tracés EEG très masqués par les artifices électromyographiques provoqués par le tremblement (surtout dans l'hémisphère gauche car il s'agit d'un hémi-Parkinson). Le dernier tracé (EMG) correspond à l'enregistrement direct de l'activité musculaire avec des électrodes superficielles posées sur le masseter (tremblement à 6 c/sec.).

B. *Une demie heure après l'injection i.v. de 20 mgr. de chlorpromazine.* Disparition presque complète du tremblement que permet d'apprécier l'activité bioélectrique cérébrale sous la forme de courbes de 50-100 μV. et fréquences de 9-10 et 15-20 c/sec. L'EMG permet d'apprécier la disparition du tremblement.

Case No. 1137

EEG records of a 44 years patient with post-encephalitic parkinsonism of 15 years duration.

A. *Before chlorpromazine.* The EEG record is masked by electromyographic artifacts provoked by the rhythmic tremor (especially on the left side). The last line (EMG), represents the direct record of the muscular activity obtained through superficial electrodes lying over the masseter muscle (rhythmic tremor at 6 c/sec.).

B. *Half an hour after the i.v. injection of 20 mgr. of chlorpromazine.* The almost complete disappearance of the tremor artifacts permits to appreciate the cerebral electrical activity characterized by 9-10 c/sec. and 15-20 c/sec. frequencies of 50-150 μV. The EMG shows the disappearance of the tremor.

DISCUSSION ET COMMENTAIRE

Les modifications psychiques observées chez les malades traités par la chlorpromazine (sédation, tranquillité, indifférence affective, lenteur dans les réponses, assoupissement facile, etc.) et qui ont déterminé les premiers essais du traitement dans le domaine de la psychiatrie ont été aussi observée au cours des recherches électrographiques que nous venons d'exposer. Au cours de celles-ci nous avons pu noter que les modifications des tracés accompagnent les modifications psychiques.

Les tracés hyperactifs et rapides, à synchronisation faible, les courbes électro-dermo-

graphiques à oscillations amples, et fréquemment l'activité électro-myographique involontaire ont correspondu à des sujets tendus et hyperexcitables. Tout ceci a été observé chez nos malades névrosés qui constituent la majorité de notre groupe.[1] L'injection de chlorpromazine a déterminé dans tous les cas un état de tranquillité et d'indifférence aux stimuli, qui était accompagné des modifications stables. L'électro-dermogramme s'est stabilisé sur la ligne de base et les artifices électromyographiques ont disparus. L'absence de modifications électrographiques à la suite des injections de sérum physiologique élimine le facteur de suggestion et d'habitude aux stimuli.

Ce parallélisme clinico-électrographique coïncide et peut s'expliquer avec les notions

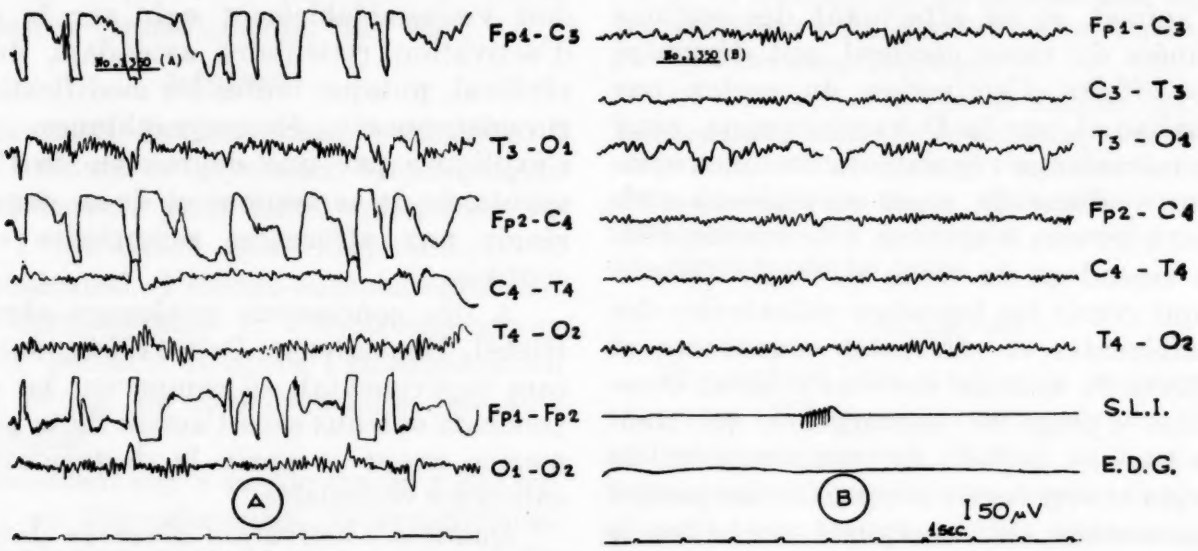

Fig. 6

Cas No 1350

Femme de 21 ans souffrant depuis 10 ans de tics généralisés mais prédominant dans la face et membres supérieurs.

A. *Avant chlorpromazine.* Les tracés sont distorsionnés par l'activité motrice involontaire surtout dans les projections frontopolaires (tics palpebraux). Le deuxième canal a été éliminé pour raisons techniques.

B. *20 min. après l'injection i.v. de 25 mgr. de chlorpromazine.* Interruption des tics avec disparition des artifices et stabilisation de l'électrodermogramme (EDG) qui ne réagit pas même à la stimulation lumineuse intermittente (SLI).

Case No. 1350

Woman, 21 years old, suffering for 10 years from generalised tics, particularily in the face and superior limbs.

A. *Before the administration of chlorpromazine.* EEG very disturbed by the involuntary motor activity especially in fronto-polar leads (tics of the eyelids). The 2nd. channel was eliminated for technical reasons.

B. *20 min. after the i.v. injection of 25 mgr. of chlorpromazine.* The tics have disappeared, the EEG artifacts have also disappeared and the electrodermographic record (EDG) shows stabilization and becomes unreactive to the flickering light (SLI).

correspondantes sur les tracés électro-encéphalographiques qui sont devenus plus synchronisés (apparition d'un rythme alpha) et plus actuelles électro-physiologiques des mécanismes nerveux qui maintiennent les états d'activité et de repos vigil. Deux groupes d'expériences ont permis l'individualisation de la substance réticulaire du tronc cérébral (hypothalamus postérieur, tegmentum mésencéphalique, protubérance et partie supérieure du bulbe) comme étant la région conditionnant le maintien de l'activité vigile de l'écorce

[1] Le Prof. Gastaut *et al.* (Marseille) a bien précisé ce type de tracé correspondant à un syndrome d'hyperexcitabilité corticale chez les sujets hyperémotifs, anxieux, etc. (voir Thèse de Le Nepvou de Carfort, 1951 et Gastaut, Roger et Roger, 1954). D'autre part Lundewold, 1952, a décrit une activité EMG exagérée chez les sujets en état de tension psychique.

cérébrale (expériences de stimulation de Moruzzi et Magoun 1949) et dont la destruction s'accompagne des manifestations électroencéphalographiques et cliniques du sommeil (Lindsley, Bowden et Magoun 1949 ; Lindsley, Schreiner, Knowles et Magoun 1950). Récemment Bonvallet, Dell et Hiebel (1954), et Hiebel, Bonvallet, Huvé et Dell (1954) en enregistrant simultanément le tracé électro-encéphalographique et la tension artérielle chez l'animal, et en effectuant des sections échelonnées du tronc cérébral, ont démontré que les effects d'activation du cortex par l'adrénaline et par la D-Amphétamine, ainsi que les mécanismes régulateurs du tonus sympathique (réflexe du sinus carotidéen) s'effectuent à travers le système d'activation réticulaire ascendant du tronc cérébral. Ce système, qui reçoit les branches collatérales des voies afférentes et efférentes somatiques et végétatives du système nerveux central, constitue une « plage de convergence qui commande tous les aspects du comportement de l'individu et représente le contrôle des parties les plus évoluées de l'encéphale sur le besoin impérieux d'intégration et de maintien de l'homéostase du milieu intérieur » (Dell 1952). Ce système multisynaptique exerce une action globale, diffuse et simultanée sur les sphères sensorielle, motrice et végétative. Son influence sur le cortex a une traduction électro-encéphalographique : l'activation du tracé lors des états d'activité vigile (tracés désynchronisés et hyperactifs) ; la synchronisation (rythmes de plus en plus lents et amples) lors du passage à l'état de repos vigil, et l'endormissement (Moruzzi 1952).

Son intervention, qui ajuste le tonus sympathique périphérique au « tonus cortical » extériorisée chez l'animal par la tension artérielle et le diamètre pupillaire (Bonvallet, Dell et Hiebel 1954) a été mise en évidence d'une façon plus simple chez l'homme par la réponse électro-dermale (Turner et Bérard 1954). Diverses expériences ont démontré l'origine centrale et la signification végétative sympathique de celle-ci (Bloch et Paillard 1951 ; Rothman 1954 ; Turner 1954).

Enfin, son effet régulateur de l'activité motrice s'exerce au moyen de connexions descendantes vers la voie finale commune (Magoun et Rhines 1949 ; Magoun 1950). De celle-ci dépendraient les variations involontaires de l'activité électro-myographique [1].

L'analyse des enregistrements électro-encéphalographiques, électro-dermographiques et électro-myographiques, obtenus avant, pendant et après l'injection de chlorpromazine permet de déduire que ceux-ci peuvent être l'expression des différents états d'activité des formations réticulaires. La chlorpromazine doit vraisemblablement agir sur le système d'activation réticulaire ascendant du tronc cérébral, puisque toutes les modifications des enregistrements électrographiques peuvent s'expliquer par une dépression de l'activité spontanée de ce système et de sa capacité de réagir aux afférences sensorielles et nociceptives.

A des conclusions analogues aboutissent Hiebel, Bonvallet et Dell (1954), sur le terrain expérimental, en comparant les enregistrements obtenus sous l'action de la chlorpromazine avant et après la destruction de la substance réticulaire.

Quant à l'activation observée dans 5 cas d'épilepsie temporale et un cas de petit mal, nous la jugeons due à l'action hypnotique de la chlorpromazine. Ainsi que l'on sait, le sommeil est une méthode d'activation de ces foyers (Fuster, Gibbs et Gibbs 1943 ; Fuster 1951).

CONCLUSIONS

1° La chlorpromazine provoque chez l'homme, en même temps qu'un état de relaxation psycho-physique, une meilleure synchronisation et régularité de l'électro-encéphalogramme, une stabilisation du tracé électro-dermographique et une diminution de l'activité électro-myographique involontaire (tension neuro-musculaire, tremblements, mouvements involontaires, etc.).

2° La chlorpromazine diminue ou annule la capacité de réagir aux divers stimuli sensoriels et noci-ceptifs comme en témoignent les électrogrammes étudiés.

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[1] Kaada (1950) a démontré que l'action de la Myanésine se réalise à travers le S.A.R.A. ; plus récemment Dell, Bonvallet et Hugelin (1954) ont démontré expérimentalement que l'adrénaline circulante exerce une action facilitatrice sur la voie finale commune à travers le S.A.R.A.

3° Toutes ces actions peuvent s'expliquer par l'action de la drogue sur le système d'activation réticulaire ascendant du tronc cérébral.

4° La chlorpromazine peut être envisagée comme un moyen d'activation de certaines formes d'épilepsie.

5° La chlorpromazine peut être aussi utilisée dans l'enregistrement EEG pour éliminer les artifices provoqués par les mouvements involontaires (tremblements, tics, etc.).

RÉSUMÉ

Les auteurs étudient chez 9 névrosés, 2 malades atteints de psychoses, 5 épileptiques psycho-moteurs, 1 petit mal, 1 épileptique végétatif, 1 Parkinson post-encéphalitique et 1 tic généralisé, l'électro-encéphalogramme, l'électro-dermogramme et l'électro-myogramme avant, pendant et après l'administration de 25 à 50 mg. de chlorpromazine par voie intra-veineuse.

Ils observent sur 8 cas de tracés EEG hyperactifs ou désynchronisés, la synchronisation et la régularisation de ceux-ci jusqu'à des fréquences proches des tracés normaux. Sur 6 cas de décharges épileptiques (5 temporales et 1 petit mal) ils ont vérifié une activation nette. Sur les tracés normaux ils n'ont pas noté des modifications importantes. Dans tous les cas étudiés, ils ont observé la stabilisation du tracé avec disparition de la réponse électrodermographique aux stimuli sensoriels, y compris les noci-ceptifs. Chez les sujets avec activité électro-myographique involontaire (tension neuro-musculaire, tics, tremblements) ils ont constaté sa diminution ou sa disparition totale pendant la demi-heure suivant l'injection de chlorpromazine. Les auteurs discutent et commentent ces recherches électrographiques à la lumière des acquisitions modernes électro-neurophysiologiques et concluent à la probable action centrale de la chlorpromazine au niveau du système d'activation réticulaire ascendant. Ils proposent la chlorpromazine pour une technique d'activation de certaines formes d'épilepsie et aussi comme moyen technique pour éliminer les artifices provoqués sur l'EEG par les mouvements involontaires.

Pendant que ce travail était sous presse, il est apparu un intéressant travail titulé: « Effect of Largactil (chlorpromazine) on Human Spasticity and Electromyogram », par J. V. Basmajian et A. Szatmari (*Arch. Neurol. Psychiat.*, Chicago, **1955**, *73*: 224-231). Les auteurs ont expérimenté l'action de cette drogue par voie intraveineuse sur des malades présentant spasticité par lésion des voies centrales de la motricité (hémiplégie vasculaire, lésions de la moelle, trauma cérébral, etc.) et dans un Parkinson, et ils observent une diminution notable de la spasticité et du tremblement. Ils arrivent donc aux résultats semblables à nos observations en ce qui concerne l'activité électromyographique.

Un autre travail de Charles Shagass (*EEG. Clin. Neurophysiol.*, **1955**, *7*: 306-308) apporte aussi les observations sur les effets de l'injection i.v. de chlorpromazine sur les tracés EEG dans 11 malades psychiatriques. Ses conclusions s'accordent en termes généraux avec les nôtres.

SUMMARY

The authors have studies the electroencephalograms (EEG), electrodermograms (EDG) and electromyograms (EMG) in 2 neurotics, 2 psychotics, 5 psychomotor epileptics, 1 case of petit mal, 1 patient with autonomic epilepsy, 1 case of post-encephalitic Parkinson, and in 1 patient suffering from generalised tic, during and after the slow intra-venous injection of chlorpromazine (4560 RP) from 25 to 50 mg.

They observed that in 8 cases of ''activated EEG pattern'' occurs the synchronization and regularization of the EEG record where the frequencies were nearly normal, i.e. alpha rhythm appeared. In 6 cases with epileptic discharges (5 temporal and 1 petit mal) a clear activation of such discharges were noted. In the normal records, no important modification occurred.

The stabilisation of the EDG was observed in every case after the injection of the drug. This was evidenced by the disappearance of oscillations in response to different sensory stimuli, including nociceptive stimuli.

In patients with involuntary electromyographic activity, (exaggerated neuro-muscular tension, tics, tremor), a decrease or total disappearance of such activity was seen during the half hour following the injection of chlorpromazine.

These results and observations are compared with recent electro-physiological findings and discussed in view of the probable central action of chlorpromazine on the brain stem reticular system. Finally chlorpromazine is proposed as a method of activation in some cases of epilepsy and also for the elimination of artifacts provoked in EEG records in cases presenting involuntary movements.

BIBLIOGRAPHIE

BLOCH, V. et PAILLARD, J. Etude polygraphique des réponses psychogalvaniques étudiées simultanément en plusieurs points du corps. *C. R. Soc. Biol.*, **1951**, *145*: 1666-1669.

BONVALLET, M., DELL, P. et HIEBEL, G. Tonus sympathique et activité électroque corticale. *EEG Clin. Neurophysiol.*, **1954**, *6*: 119-144.

CASTRO, P. DE y BÉRARD, E. Efectos del Clorhidrato de Cloro-3(dimetilamino-3-propil) 10 fenotiazina (4.560 R.P.) sobre el electroencefalograma. *EEG Clin. Neurophysiol.*, **1954**, *6*: 340.

DELL, P. Corrélations entre le système végétatif et le système de la vie de relation. Mésencéphale, diencéphale et cortex cérébral. *J. Physiol.*, Paris, **1952**, *44*: 471-557.

DELL, P., BONVALLET, M. et HUGELIN, A. Tonus sympathique, adrénaline et contrôle réticulaire de la motricité spinale. *EEG Clin. Neurophysiol.*, **1954**, *6*: 599-618.

FUSTER, B. Efecto del sueño inducido con diferentes drogas, sedantes, hipnóticos y anticonvulsivantes sobre el electroencefalograma en la epilepsia psicomotriz. *Arch. Uruguayos de Med. Cir. y esp.*, Montevideo, **1951**, *39*: 245-270.

FUSTER, B., GIBBS, E. L. and GIBBS, F. A. Pentothal sleep as an aid to the diagnosis and localization of seizures discharges of the psychomotor type. *Dis. nerv. Syst.*, **1948**, *9*: 199-202.

GASTAUT, H., ROGER, A. et ROGER, J. De l'intérêt de l'EEG dans les indications de la cure de sommeil. *La Cure de Sommeil*, Paris, Masson et Cie., **1954**, I vol., 238 pp.

HIEBEL, G., BONVALLET, M. et DELL, P. Action de la chloropromazine (Largactil 4560 RP) au niveau du système nerveux central. *S. Hôp.*, Paris, **1954**, *30*: 2346-2353.

HIEBEL, G., BONVALLET, M., HUVE, P. et DELL, P. Analyse neurophysiologique de l'action centrale de la d-amphétamine (Maxiton). *Sem. Hôp.*, Paris, **1954**, *30*: 1880-1887.

KAADA, B. R. Site of action of Myanesin (Mephenesin, Tolserol) in the central nervous system. *J. Neurophysiol.*, **1950**, *13*: 89-103.

LE NEPVOU DE CARFORT. Etude EEG du syndrome d'hiperexcitabilité neuronique. *Thèse*, Marseille, **1951**.

LINDSLEY, D. B., BOWDEN, J. W. and MAGOUN, H. W. Effect upon the EEG of acute injury of the brain stem activating system. *EEG Clin. Neurophysiol.*, **1949**, *1*: 475-486.

LINDSLEY, D. B., SCHREINER, L. H., KNOWLES, W. B. and MAGOUN, H. W. Behavioral and EEG changes following chronic brain stem lesions in the cat. *EEG Clin. Neurophysiol.*, **1950**, *2*: 483-498.

LUNDEWOLD, A. An EMG investigation of tense and relaxed subjects. *J. nerv. ment. Dis.*, **1952**, *115*: 512-525.

MAGOUN, H. W. Caudal and cephalic influences of the brain stem reticular formation. *Physiol. Rev.*, **1950**, *30*: 459-474.

MAGOUN, H. W. and RHINES, R. Spasticity. The stretch reflex and extrapyramidal systems. Charles Thomas, Springfield (Ill.), **1949**, 59 pp.

MORUZZI, G. Il problema fisiologico del sonno. *Minerva Med.*, **1952**, *1*: 730-734.

MORUZZI, G. and MAGOUN, H. W. Brain stem formation and activation of the EEG. *EEG Clin. Neurophysiol.*, **1949**, *1*: 455-473.

ROTHMAN, S. *Physiology and Biochemistry of the Skin.* The University of Chicago Press, **1954**, 471 pp.

TERZIAN, H. Studio elettroencef. del l'azione centrale del largactil (4560 RP). *Rass. Neur. Vegetative*, **1952**, *9*: 211-215.

TERZIAN, H. Etude EEG de l'action centrale de la chloropromazine (4560 RP). *S. Hôp.*, Paris, **1954**, *30*: 838-844.

TURNER, M. El electrodermograma (EDG) como técnica de estudio de la respuesta emocional periférica (reflejo psicogalvánico). *Rev. Neuro-Psiquiatría*, Lima (Pérú), **1954**, *17*: 235-239.

TURNER, M. et BÉRARD, E. Etude sur les effets de la Chloropromazine (4560 R.P.) sur les tracés électroencéphalographiques et électrodermographiques. *EEG Clin. Neurophysiol.*, **1954**, *6*: 538.

TURNER, M. y BÉRARD, E. Estudio del efecto de la cloropromazina (4560 RP) sobre el electroencefalograma y el electrodermograma. *Bol. Soc. Arg. Biol.*, Buenos Aires, **1954** (sous presse).

Reference: TURNER, M., BÉRARD, E., TURNER, N. et FRANCO, N. Modifications électro-encéphalographiques, électro-dermographiques et électro-myographiques provoquées par le chlorpromazine chez l'homme. *EEG Clin. Neurophysiol.*, **1956**, *8*: 25-34.

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MODIFICATIONS DE L'ÉLECTRO-DERMOGRAMME, DE LA SUDATION ET LA TEMPÉRATURE CUTANÉE PROVOQUÉES PAR LA CHLORPROMAZINE (4560 R.P.) CHEZ L'HOMME

NELLY A. CLERC, MARCOS TURNER et ENRIQUE BÉRARD
Laboratorio de Electroneurofisiología Clínica, Buenos Aires, Argentina

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INTRODUCTION

L'emploi de la chlorpromazine (4560 RP) dans les traitements neuroplégiques, d'application de plus en plus courante, a provoqué toute une série de recherches tendant à éclaircir sa pharmacodynamie.

La peau étant un organe riche en manifestations végétatives, nous avons essayé de rechercher au moyen de diverses techniques les effets que l'administration de ce neurolytique y produit, et d'interpréter ainsi son mécanisme d'action.

MATÉRIEL ET MÉTHODES

Les recherches ont eu lieu sur 5 sujets adultes, des deux sexes, à peau apparemment normal, à demi-assis, habillés et placés à une température ambiante de 25° à 28° C.

On a employé la chlorpromazine à la dose de 50 mgr. diluée dans 20 cc. de sérum physiologique, en injection intra-veineuse lente (10 à 15 min.).

On a effectué l'enregistrement de l'EDG (électro-dermogramme) en plaçant deux électrodes, une sur la paume et l'autre sur le dos de la main, et en les branchant sur une chaîne d'amplification d'un électroencéphalographe Kaiser, en employant une constante de temps de 0,6 sec. et une amplification adéquate (technique de Bloch-Paillard, 1951).

Pour la *sudation* on a stimulé la face de flexion de l'avant-bras, au tiers supérieur. Nous avons fait une injection intra-dermique de 0,1 cc. d'une solution de chlorure d'adrénaline 1/1000 et de 0,1 cc. d'une solution de carbaminoilcoline (Doryl), à la dose de 0,02 mg.

On a procédé à l'enregistrement de la sueur provoquée par l'adrénaline au bout de 3 min., moment de l'effet maximum. Quant au Doryl, au bout de 2 min. on obtient déjà la sécrétion de sueur maximum, qui persiste longtemps car la drogue n'est pas détruite par la cholinestérase (Lobitz et Campbell 1953).

Aux endroits des injections nous avons appliqué, après une période d'attente nécessaire, le papier indicateur que nous avons laissé en place pendant 30 sec. Ce papier est un papier de filtre, libre de sels, du type Whatmann # 2 (Balston, England), découpé en morceaux de 1 x 3 cm. Il est traité avec une poudre adhérente dont l'élément principal est le bleu de bromophénol, dans un mélange de carbonate soude, d'amidon de pomme de terre et de gomme Karaya. Le principe du test est basé sur un changement de la couleur du papier, d'une couleur blanc à un bleu pâle ou foncé. La présence de l'eau est une condition indispensable pour ce changement (méthode de Jadasshon-Manuila) (Herrmann, Prose, Sulzberger 1951).

Après cet enregistrement nous avons attendu 10 min. puis nous avons répété l'application des papiers indicateurs aux mêmes endroits pendant 30 sec., *tout en stimulant le bras opposé avec un instrument aigu et avec une pression modérée* (provocation du stimulus nociceptif controlateral).

On a effectué ces épreuves avant et après l'injection intra-veineuse de chlorpromazine.

La *température cutanée* a été obtenue avec le Mac Kesson Dermalor, d'une haute sensibilité. On a enregistré la température cutanée et la température ambiante d'une façon presque simultanée. On a examiné la température à la joue, au bras (face antérieure), au dos de la main et à la jambe (tiers inférieur et

externe), avant et après l'injection du 4560 RP. Les enregistrements ont été pris 5,20 et 30 min. après l'injection. Pour contrôler les résultats on a obtenu les degrés de différence entre l'ambiance et la température cutanée locale, température différentielle donnant un indice sur la variation enregistrée.

RÉSULTATS OBTENUS

Epreuves de sudation. La quantité d'eau enregistrée en tant que sueur a été moindre chez la femme. Ceci concorde avec la description de Herrman et Sulzberger (1952). Après l'injection intradermique d'adrénaline nous avons constaté dans tous les cas une zone de vaso-constriction due à l'action vasomotrice directe de la drogue. Cette zone s'est étendue périphériquement à la façon de pseudopodes (diffusion par voie lymphatique). La sueur est apparue dans la zone de vaso-constriction d'une façon modérée. La réponse obtenue après le stimulus noci-ceptif a été quantitativement plus importante. L'administration du 4560 RP a fait disparaître la réponse sudorifique dans tous les cas. Ce résultat a été constant. *La stimulation noci-ceptive contralatérale effectuée dans un but de contrôle nous a permis d'enregistrer avec les papiers indicateurs une faible sudation* (fig. 1).

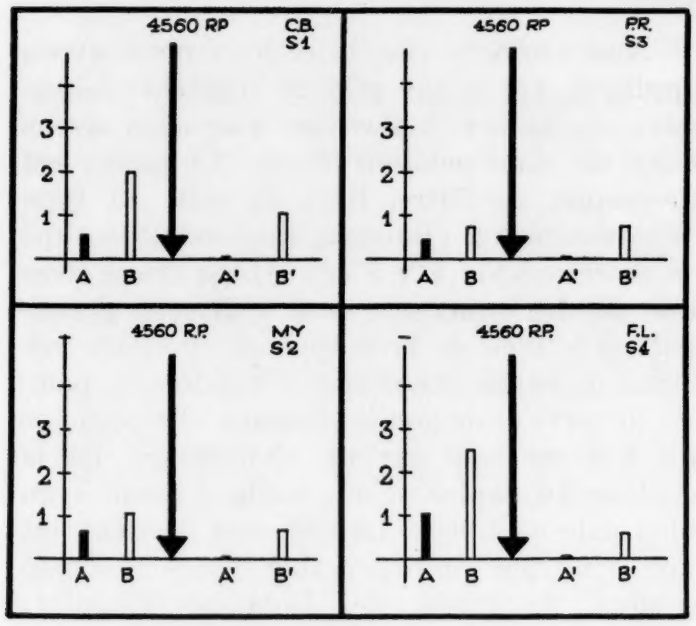

Fig. 1

Réaction sudorifique à l'adrénaline.

Ordonnées. Echelle conventionnelle de quantité de sueur éliminée.

A. Réaction à l'injection intradermique d'adrénaline.
B. Réaction du même point en ajoutant un stimulus noci-ceptif du côté opposé.
A'. Idem à A, 20 min. après l'injection intraveineuse de chlorpromazine (4560 RP).
B'. Idem à B, 30 min. après l'injection i.v. de chlorpromazine.

Sudorific response to adrenalin.

Ordinates. Conventional scale of quantities of sweat.

A. Response to the intradermic injection of adrenalin.
B. Response at the same place after a nociceptif opposite side stimulation.
A'. Idem A, 20 min. after the i.v. injection of chlorpromazine (4560 RP).
B'. Idem B, 30 min. after the i.v. injection of chlorpromazine (4560 RP).

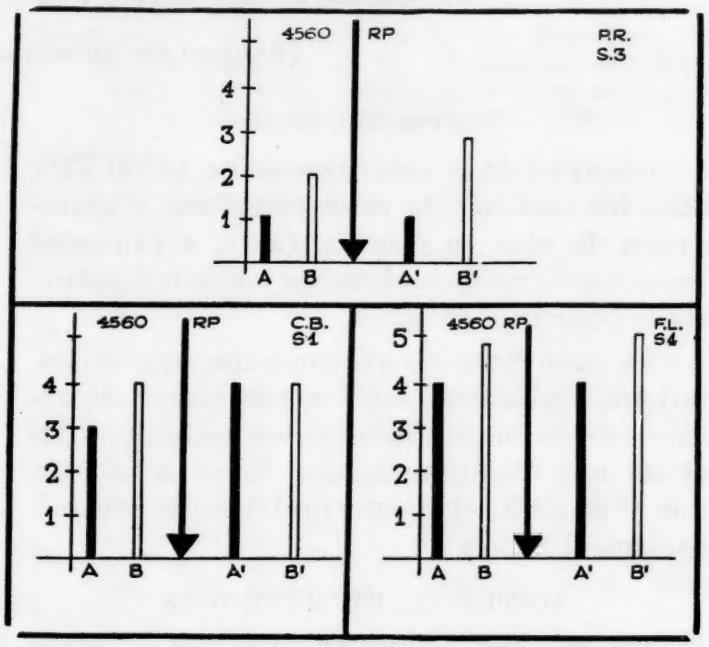

Fig. 2

Réaction sudorifique au Doryl (carbaminoilcoline).

Ordonnées. Echelle conventionnelle de quantité de sueur éliminée.

A. Réaction à l'injection intradermique de Doryl (carbaminoilcoline).
B. Réaction du même point en ajoutant un stimulus noci-ceptif du côté opposé.
A'. Idem A, 20 min. après l'injection i.v. de chlorpromazine (4560 RP).
B'. Idem B, 30 min. après l'injection i.v. de chlorpromazine (4560 RP).

Sudorific response to Doryl (carbaminoilcoline).

Ordinates. Conventional scale of quantities of sweat.

A. Response to the intradermic injection of Doryl (carbominoilcoline).
B. Response at the same place after the nociceptif stimulation on the opposite side.
A'. Idem A, 20 min. after the i.v. injection of chlorpromazine (4560 RP).
B'. Idem B, 30 min. after the i.v. injection of chlorpromazine (4560 RP).

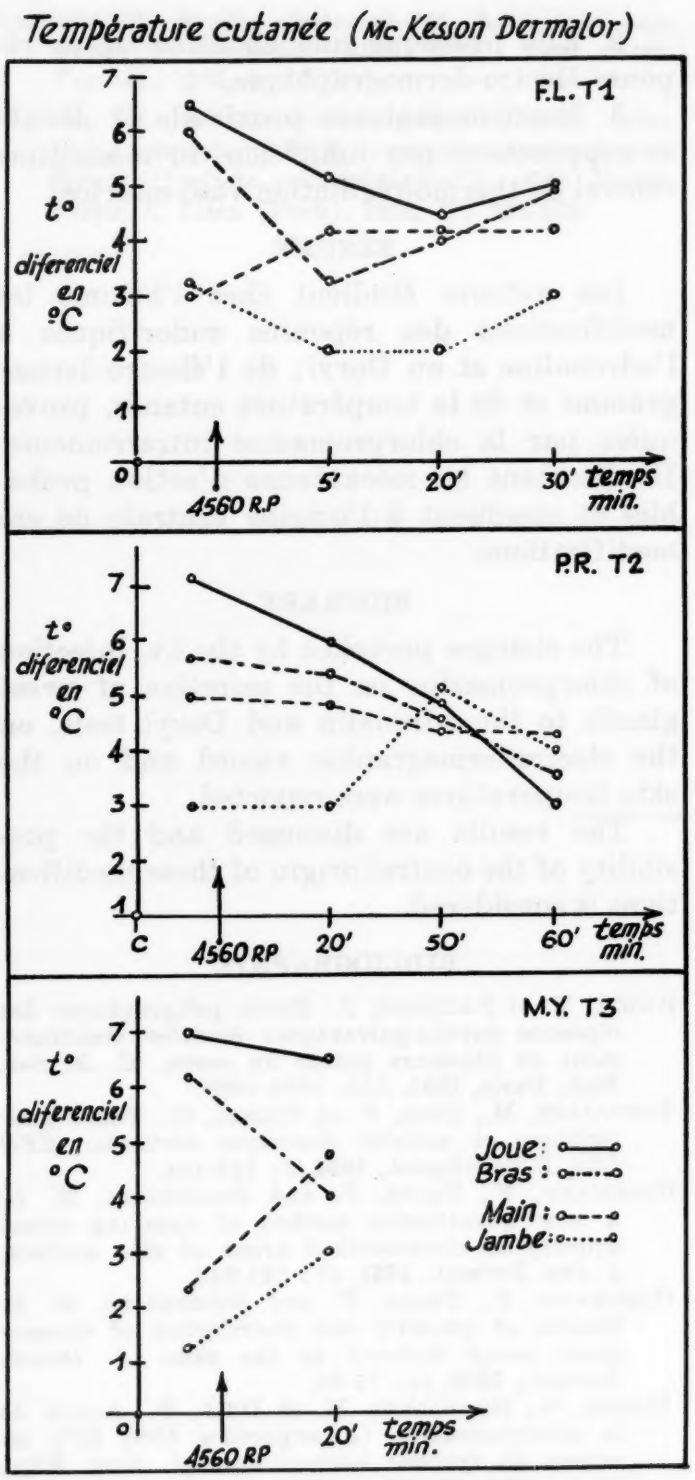

Fig. 3

Graphique des températures cutanées différentielles.
Abcises. Temps en minutes.
Ordonnées. Température différentielle entre l'air ambiant et la surface cutanée, exprimée en centigrades.

Graphic of the skin differential temperatures.
Abcisses. Time in minutes.
Ordinates. Differential temperatures between ambiant air and skin surface, expressed in centigrades.

La stimulation par la carbaminoilcoline a produit un effet vasodilatateur immédiat, résultat d'un réflexe axonique. Nous avons observé également le réflexe pilo-moteur et la sécrétion de sueur.

A la première épreuve, nous avons obtenu dans trois cas une augmentation de la réponse au stimulus noci-ceptif controlatéral. Après l'injection d'Ampliactil, la stimulation intra-dermique ne donne pas de résultat similaire, *bien que le stimulus noci-ceptif controlatéral a provoqué une augmentation dans deux cas* (fig. 2).

Enregistrement de la température: Quant à la température on a constaté qu'après l'administration du 4560 RP, la température différentielle de la joue et du bras (régions que nous appellerons proximales) a diminué dans tous les cas, diminution toujours en rapport direct avec la température différentielle du premier enregistrement. Au contraire la température différentielle de la main et de la jambe (régions distales) a subi une augmentation, qui dans un cas a fait coïncider la température des régions proximales et distales (fig. 3).

Enregistrement de l'EDG. L'enregistrement avant l'injection du 4560 RP a montré d'amples variations aux stimuli psychiques et émotifs (clap, piqûres, stimuli lumineux, appel par le nom, etc.). Après l'injection aucun des stimuli appliqués n'a provoqué de réponse électro-dermographique.

COMMENTAIRE

En tenant compte de l'exposé des paragraphes antérieurs et en réunissant les données obtenues, nous voulons attirer l'attention sur le fait qu'au cours des épreuves de sudation, la réponse adrénergique après l'injection de chlorpromazine a été constamment négative.

Etant donné l'innervation des glandes sudoripares par des filets parasympathiques cholinergiques et sympathiques cholinergiques, et les études tendant à prouver également l'existence d'une innervation sympathique adrénergique, ces résultats suggèrent que :

Le 4560 RP est un sympathicolytique d'action adrénolytique, qui produirait l'inhibition de la réponse sudorifique adrénergique. *Cependant la stimulation noci-ceptive controlatérale stimule la réponse à l'épreuve de l'adrénaline.* Les réponses sudorifiques se font à travers *un réflexe court et médullaire* (elles persistent malgré la section haute de la moelle, Richter 1930), et un *réflexe long* avec intervention du mésencéphale et du cortex (elles disparaissent après l'ablation corticale, Schwartz 1937). Le réflexe court expliquerait la persistence de la réponse à la stimulation noci-ceptive controlatérale. L'abolition de la réponse à l'adrénaline intradermique indiquerait un blocage du réflexe long ou central par la chlorpromazine. Ce phénomène correspond à la disparition de la réponse de l'EDG. En accord avec les fonctions des glandes sudoripares, on observe que la sudation est provoquée aux mains par l'activité, l'attention, le travail mental et l'émotion (Lobitz et Osterberg 1945). La réponse EDG est déterminée par une modification de l'activité sudorifique palmaire répondant de préférence à l'état émotif, où interviennent les arcs réflexes supérieurs par voie sympathique (Bloch et Paillard 1951; Rothman 1954; Turner 1954). L'inhibition de cette réponse est compréhensible en tenant compte de l'action centrale de la chlorpromazine, démontrée ou supposée par les résultats obtenus avec d'autres techniques électro-physiologiques (Bonvallet, Dell et Hiebel 1954; Hiebel, Bonvallet et Dell 1954; Terzian 1952; Turner et Bérard 1954).

Les modifications de la température cutanée, plus importantes aux régions distales, indiquerait aussi une action sur les centres nerveux intervenant sur les mécanismes vasomoteurs de la thermo-régulation (Rothman 1954). La drogue en éliminant ce mécanisme d'origine centrale, qui chez l'homme s'extériorise tout spécialement aux extrémités des membres, provoque le rapprochement des températures proximales et distales.

CONCLUSIONS

1. La chlorpromazine produit une inhibition de la réponse sudorifique adrénergique d'origine centrale.

2. Elle provoque une abolition de la réponse électro-dermographique.

3. Les températures proximale et distale se rapprochent par inhibition du mécanisme central de thermo-régulation vaso-motrice.

RÉSUMÉ

Les auteurs étudient chez l'homme les modifications des réponses sudorifiques à l'adrénaline et au Doryl; de l'électro-dermogramme et de la température cutanée, provoquées par la chlorpromazine intra-veineuse. Ils discutent les mécanismes d'action probables et concluent à l'origine centrale de ces modifications.

SUMMARY

The changes provoked by the i.v. injection of chlorpromazine on the secretion of sweat glands to the adrenalin and Doryl tests, on the electrodermographic record and on the skin temperatures were reported.

The results are discussed and the possibility of the central origin of these modifications is considered.

BIBLIOGRAPHIE

BLOCH, V. et PAILLARD, J. Etude poligraphique des réponses psycho-galvaniques étudiées simultanément en plusieurs points du corps. *C. R. Soc. Biol.*, Paris, **1951**, *145*: 1666-1669.

BONVALLET, M., DELL, P. et HIEBEL, G. Tonus sympathique et activité électrique corticale. *EEG Clin. Neurophysiol.*, **1954**, *6*: 119-144.

HERRMANN, F., PROSE, P. and SULZBERGER, M. B. A new quantitative method of assaying sweat delivery to circunscribed areas of skin surface. *J. Inv. Dermat.*, **1951**, *17*: 241-248.

HERRMANN, F., PROSE, P. and SULZBERGER, M. B. Studies of quantity and distribution of thermogenic sweat delivery to the skin. *J. Invest. Dermat.*, **1952**, *18*: 71-86.

HIEBEL, G., BONVALLET, M. et DELL, P. Action de la chlorpromazine (« Largactil » 4560 RP) au niveau du système nerveux central. *Sem. Hôp.*, Paris, **1954**, *30*: 2346-2353.

LOBITZ, W. and OSTERBERG, A. Chemistry of palmar sweat. Preliminary report. *J. Investig. Dermat.*, **1945**, *6*: 63-73.

LOBITZ, W. and CAMPBELL, C. Physiologic studies on atopic dermatitis. *Arch. Derm. Syphil.*, **1953**, *67*: 574-584.

RICHTER, C. P. Galvanic skin reflex from animals with complete transection of the spinal cord. *Amer. J. Physiol.*, **1930**, *93*: 468-472.

ROTHMAN, S. *Physiology and biochemistry of the skin.* Chicago University Press, **1954**, 741 pp.

SCHWARTZ, H. G. Effect of experimental lesions of the cortex on the psychogalvanic reflex of the cat. *Arch. Neurol. Psychiat.*, Chicago, **1937**, *38*: 308-320.

TERZIAN, H. Studio elettroencefal. dell'azione centrale del Largactil (4560 RP). *Rass. Neur. Vegetat.*, **1952**, *9*: 211-215.

TURNER, M. El electrodermograma (EDG) como técnica de estudio de la respuesta emocional periférica (''reflejo psicogalvánico''). *Rev. Neuro-Psiquiat.*, Lima (Perú), **1954**, *17*: 235-239.

TURNER, M. et BÉRARD, E. Etude sur les effets de la Chlorpromazine (4560 RP) sur les tracés électro-encéphalographiques et électrodermographiques. *EEG Clin. Neurophysiol.*, **1954**, *6*: 538.

TURNER, M. y BÉRARD, E. Estudio del efecto de la cloropromazina (4560 RP) sobre el EEG y el EDG. *Bol. Soc. Arg. Biol.*, Buenos Aires, **1954** (sous presse).

Reference: CLERC, NELLY A., TURNER, MARCOS et BÉRARD, ENRIQUE. Modifications de l'électro-dermogramme, de la sudation et la température cutanée provoquées par la chlorpromazine (4560 R.P.) chez l'homme. *EEG Clin. Neurophysiol.*, **1956**, *8*: 35-39.

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ANNOUNCEMENT

INTERNATIONAL EUROPEAN EEG MEETING

An International Meeting of the European EEG Societies is to be held on 24-25-26th May, 1956 at the Royal College of Surgeons of England in London. Provisionally, two topics are to be discussed:

1. Instrumentation, recording and processing methods.

2. EEG and Pharmacology.

Organizing Committee:	W. Grey Walter.
	W. A. Cobb.
	S. L. Sherwood.
Honorary Advisers:	F. Buchthal.
	H. Fischgold.
	H. Gastaut.

A COMPARISON OF HYPERVENTILATION AND APNOEA ACTIVATION OF THE EEG[1]

DANIEL SILVERMAN, M.D.

With the technical assistance of T. SANNIT, B.S. and S. PIWOZ, B.A.

Department of Neurology, Graduate School of Medicine, Graduate Hospital, University of Pennsylvania, Philadelphia, Pa.

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This investigation is based on Lloyd-Smith's (1950) observation that subjects undergoing electroencephalographic examination can be persuaded, after a period of hyperventilation, to hold their breath long enough to produce EEG slowing, accompanied usually by observable cyanosis. Lloyd-Smith was concerned in his study with the mechanism producing bradyrhythmia during hyperventilation and was led to suggest that the more responsible factor was hypoxia rather than hypocapnia; he did note, however, that apnoea precipitated paroxysmal abnormalities in several epileptics. Bickers (1953) pursued the matter further, examined 150 patients and concluded that apnoea may be a useful activation procedure in some cases. This study was undertaken to explore in a more definitive way the practical value of apnoea following hyperventilation as a technique of activation.

METHOD

One thousand consecutive patients who were being studied electrographically at the Graduate Hospital EEG Laboratory were instructed to hold their breath immediately after a routine 2 to 3½ min. hyperventilation. The patient was told that this was a most important part of his test, reassured that no harm might result from the procedure, advised that if necessary to help him maintain the apnoea he could hold his nostrils while his mouth was closed and that he should keep this up until the technician indicated when normal breathing could be resumed. If the patient felt his limit had been reached, he was instructed to signal the technician by raising a hand; if the EEG response was not yet adequate, he was encouraged to maintain apnoea longer. Patients were watched carefully for involuntary breathing and for cyanosis. Attempts at apnoea of less than 1 min. were not included in the final correlative data of this study, inasmuch as this was the minimum time that changes attributable to apnoea were found. In most cases 1½ min. of apnoea were required to produce definite effects. In each case the response to apnoea was compared to the response to hyperventilation; the results were then correlated with the patient's age, EEG classification, clinical diagnosis and EEG diagnostic value.

RESULTS

Of the 1,000 patients, 213 could not or would not hold their breath for a minimum of 1 min., in contrast with 136 who did not satisfactorily perform hyperventilation. Inadequate hyperventilation and apnoea were due principally to immaturity or to physical or mental factors (debilitation, confusion or coma) which precluded satisfactory cooperation. The youngest able to produce a minimum period of apnoea was 6 years; the youngest to hyperventilate adequately was 3 years.

Of the patients who cooperated, 311 showed no changes during hyperventilation and 480 none during apnoea. A variety of EEG changes were observed in the remainder. The most common response was a slowing of comparable degree in the 2-4 c/sec. range with both procedures. Hyperventilation ordinarily was associated with a gradual increase in slow frequencies, followed by a return to the pre-overbreathing record during early apnoea

[1] Presented as a scientific exhibit at the June 1955 meeting of the American Electroencephalographic Society.

and then, after 1 to 1½ min., a recurrence of the slow frequencies, which finally rapidly disappeared after a few normal breaths (fig. 1). At times the slowing produced by apnoea hyperventilation was pronounced while during apnoea the response was mild or nil. The next most common response was slowing of comparable degree in the 5-7 c/sec. range

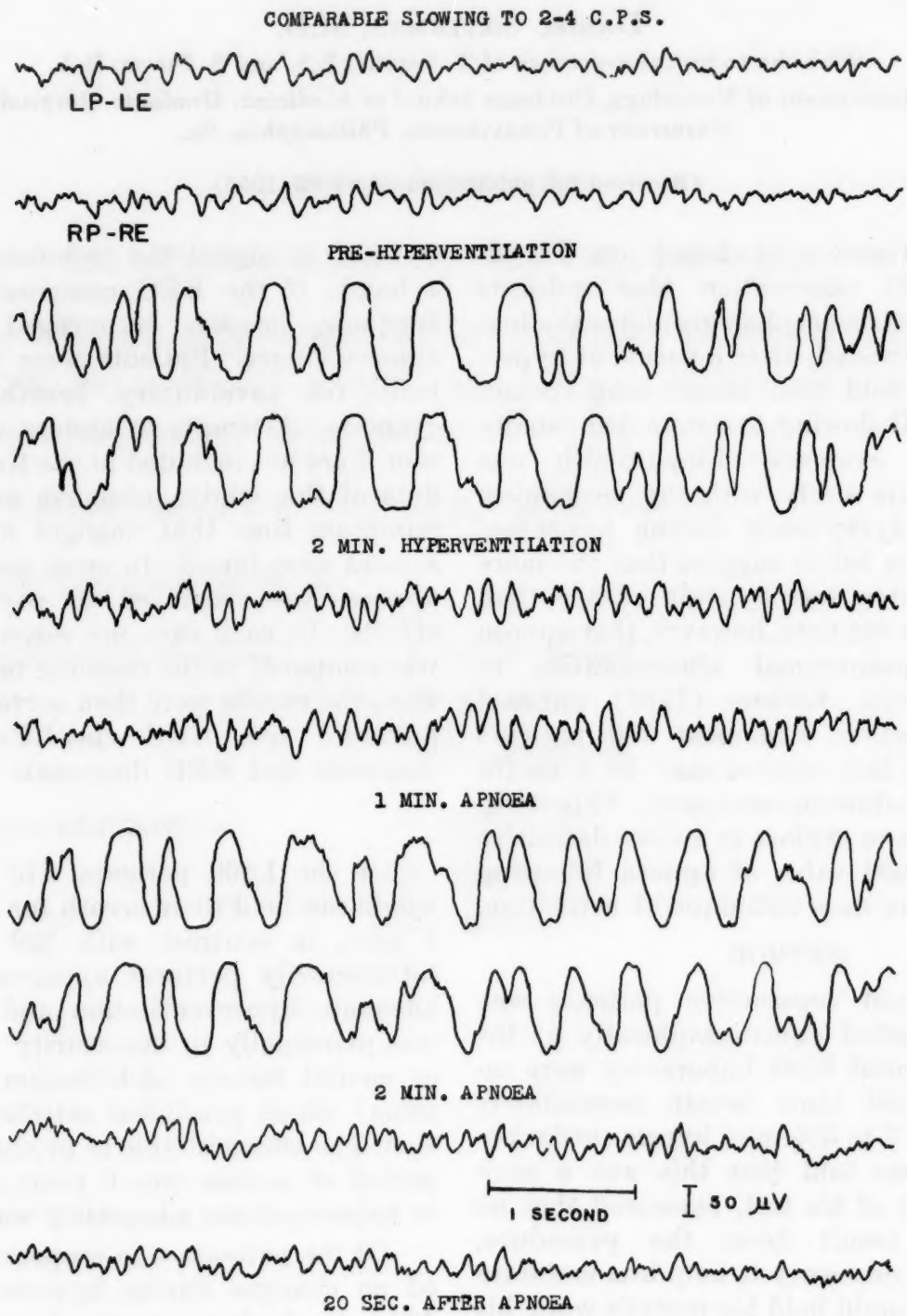

Fig. 1

was more pronounced (fig. 2); more often the changes resulting from hyperventilation exceeded those which occurred during apnoea (fig. 3). Not infrequently the slowing during with both procedures; there was the same variability as mentioned above with respect to the slowing in the 2-4 c/sec. range. Focal slow or sharp waves and focal spikes or

spike-waves were elicited in 62 hyperventilations and in 54 apnoeas. Not infrequently both procedures were similarly effective, but at times one gave a pathologic response and the other either no response or generalized slowing; an example is given in figure 4. Generalized paroxysmal bursts of 3 c/sec. waves, spikes or spike-waves were brought out in 53 hyperventilations in contrast to 21 apnoeas; an example is given in figure 5. It was rare for the generalized paroxysmal response to

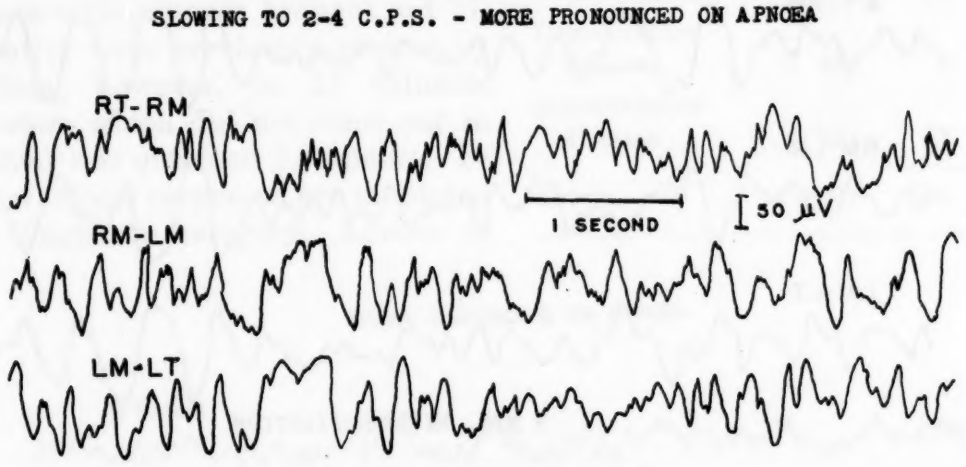

Fig. 2

be elicited on apnoea without its having been produced previously on hyperventilation.

Figures 6 and 7 illustrate the effect of age on the types of response in those who were able to perform the activations. EEG slowing from 2 to 4 c/sec. during hyperventilation was most closely related to age; this inverse relationship held until the senile group was reached. Slowing during apnoea followed the curve of hyperventilation, but at a lower level of effectiveness. The 53 paroxysmal responses to hyperventilation (including 27 generalized spike-waves) were also more common in the younger. Slowing to 5 to 7 c/sec. and focal abnormalities did not follow a linear age curve.

Slowing in the 2 to 4 c/sec. range during hyperventilation is not usually considered a criterion for EEG abnormality; in only 4 cases, where this effect was most pronounced and persistent afterwards, was this slowing in itself deemed pathologic. In 2 of the latter cases there was a similar slowing during apnoea. Figure 8 shows the activation responses recorded according to EEG classifica-

tion. It will be seen that there was a trend toward more 2 to 4 c/sec. slowing in the non-focal abnormal EEG's than in the normal EEG's. There was no question that paroxysmal and focal changes during activation were pathologic.

When the clinical diagnosis was considered, it was found that almost all the paroxysmal and slightly less than half the focal activation responses occurred in those with seizures. The remainder of the focal responses was distributed among the tumors and tumor suspects, vascular and post-traumatic conditions. Although slowing in the 2 to 4 c/sec. range occurred somewhat more commonly in patients with epilepsy, tumors and miscel-

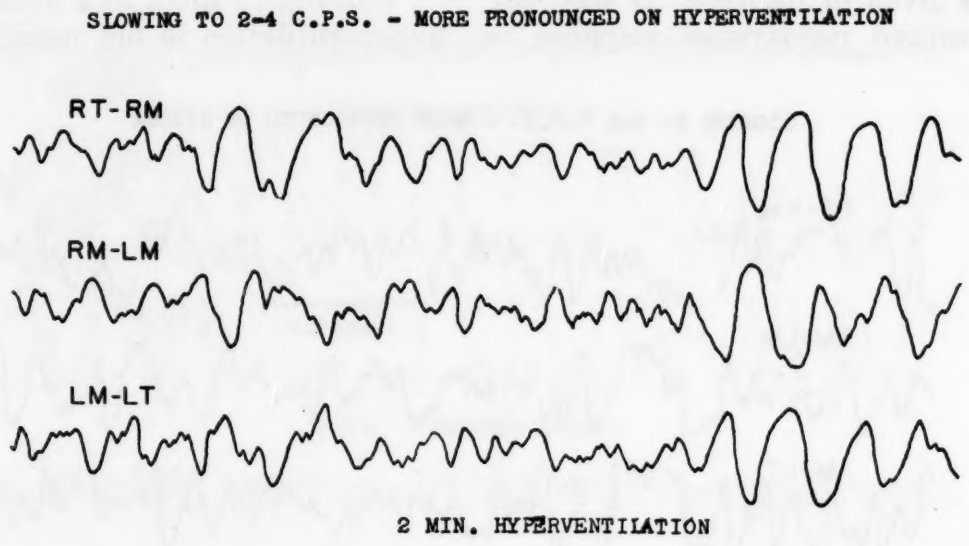

Fig. 3

TABLE I

PATHOLOGIC RESPONSES

	1. Contributory			2. Significant			
	Both	HV alone	Apnoea alone	Both	HV alone	Apnoea alone	Total
Pathologic slow	2	2	0	0	0	0	4
Focal	31	21	9	7	3	7	78
Paroxysmal	7	19	1	11	16	2	56
Totals	40	42	10	18	19	9	138

laneous diseases, such slowing was of no value for purposes of differential diagnosis.

Table I lists the pathologic responses that were of contributory and of significant value in the EEG diagnosis. A contributory response is defined as one that confirmed what might have also appeared in the resting, sleep or photic stimulation recording, whereas the significant response was more crucial for the EEG diagnosis, having appeared not at all or only suggestively in the remainder of the record. Hyperventilation produced 119 pathologic responses while apnoea brought out 77. Most of the latter were previously elicited by hyperventilation; however, in 19 valuable EEG information which did not come out in hyperventilation was obtained by apnoea. In table II the pathologic responses are tabulated according to diagnostic category. Apnoea as

TABLE II
PATHOLOGIC RESPONSES

		HV or both	%	Apnoea alone	%
Epilepsies	(300)	93	(67)	12	(63)
Functional disorders	(211)	2	(2)	0	
Brain tumor and tumor suspects	(136)	13	(9)	3	(16)
Vascular diseases	(119)	8	(6)	1	(5)
Brain trauma	(99)	18	(13)	3	(16)
Degenerative diseases	(49)	1	(1)	0	
Miscellaneous diseases	(86)	3	(2)	0	
Totals	(1000)	138	(100)	19	(100)

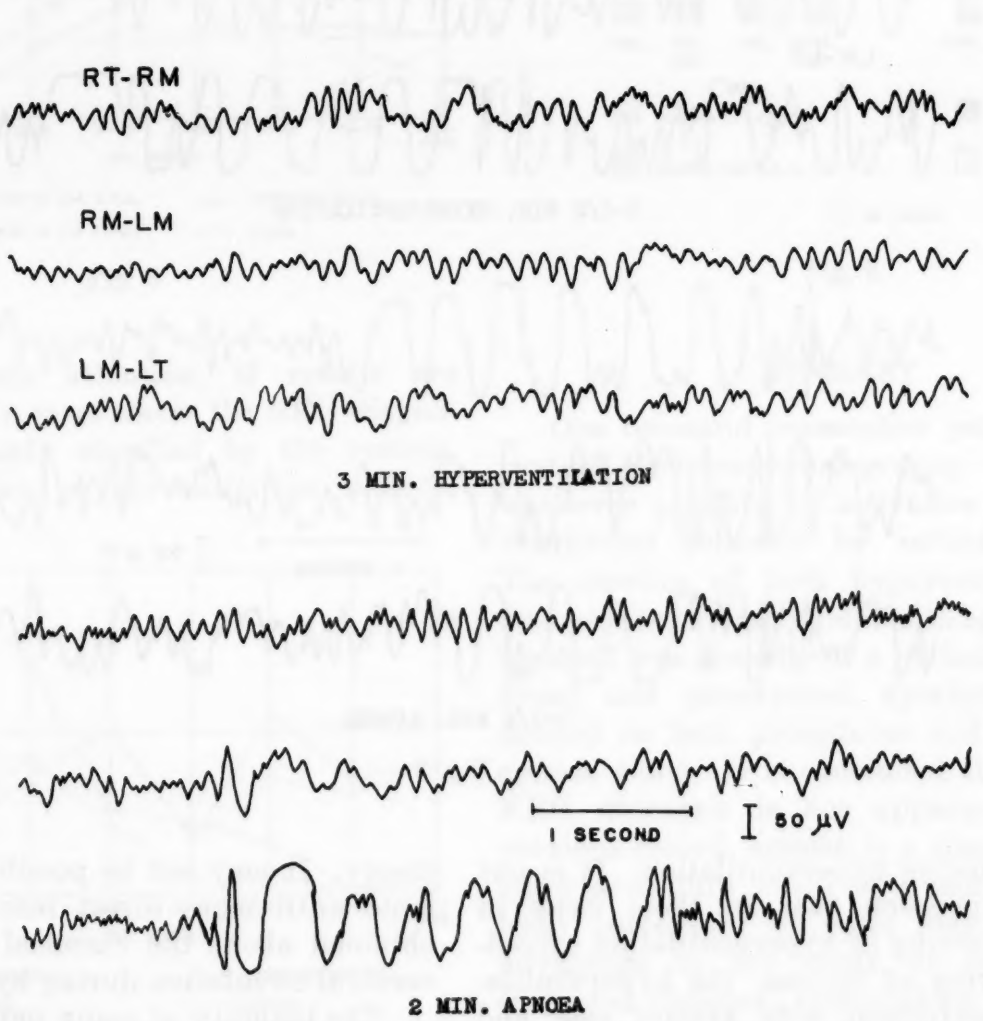

Fig. 4

well as hyperventilation had its maximum usefulness in the study of the epilepsies. Though less effective, it was still of value in the examination of brain tumors, tumor suspects, cerebral trauma and vascular disorders.

DISCUSSION

This study amply confirms Lloyd-Smith's findings (*op. cit.*) of bradyrhythmia on apnoea following hyperventilation. It is our distinct impression that in those cases in whom the slowing of hyperventilation exceeded the slowing of apnoea, the hyperventilation was performed with greater ease and more effectively, and that this explained the difference in the results obtained. It was not our objective, however, either to quantitate the effects of these activation techniques or to clarify the hypoxia-hypocapnia controversy. The parallels in the responses to the two activations are not conclusive evidence for the hypoxia theory and as Hulmberg (1953) pointed out, there is a body of data which indirectly supports the hypocapnia theory. It may not be possible to decide this issue until more direct information can be obtained about the chemical changes in the cerebral circulation during hyperventilation.

The inability of many patients to perform effective apnoea limits the usefulness of the

PAROXYSMAL RHYTHMS ON HYPERVENTILATION AND APNOEA

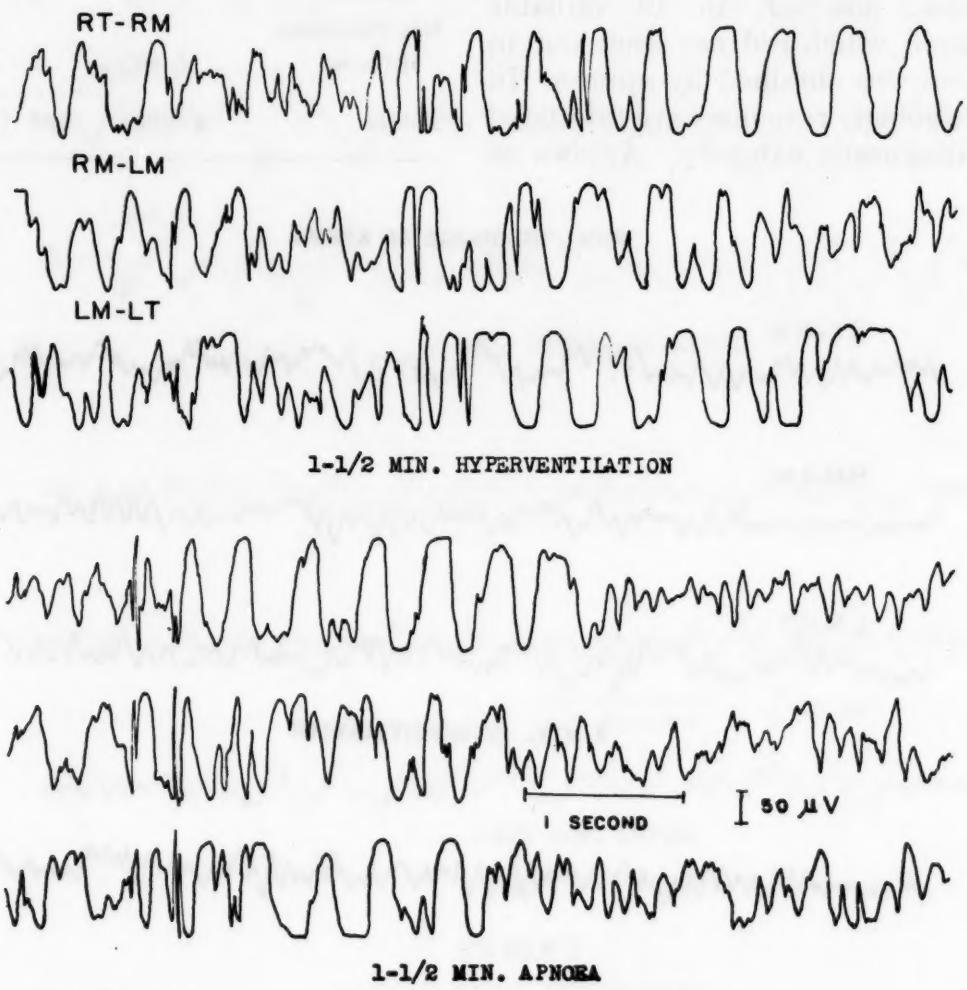

Fig. 5

procedure; 69 per cent of patients in this series were unable to produce changes during apnoea, as compared to 45 per cent of patients with hyperventilation. Yet the simplicity, safety and rapidity of this activation technique commands attention, if results are forthcoming. In cases where the EEG diagnosis is not already clarified by the resting, sleep, photic and hyperventilation records, apnoea activation is a valuable and recommended procedure. This is especially true in all patients who are afflicted with epileptic seizures. Apnoea is less useful but still of some value in cases of space-taking lesions, vascular disorders and post-traumatic states.

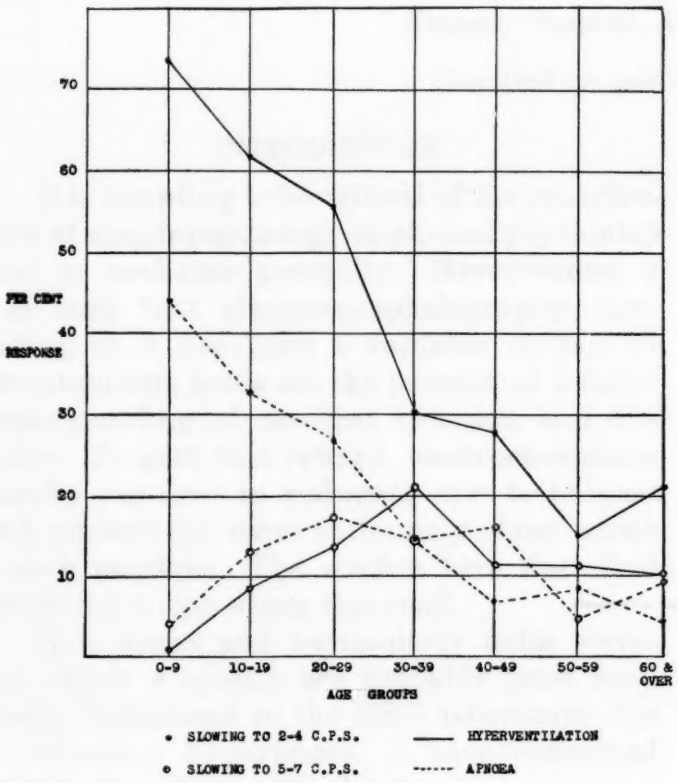

Fig. 6

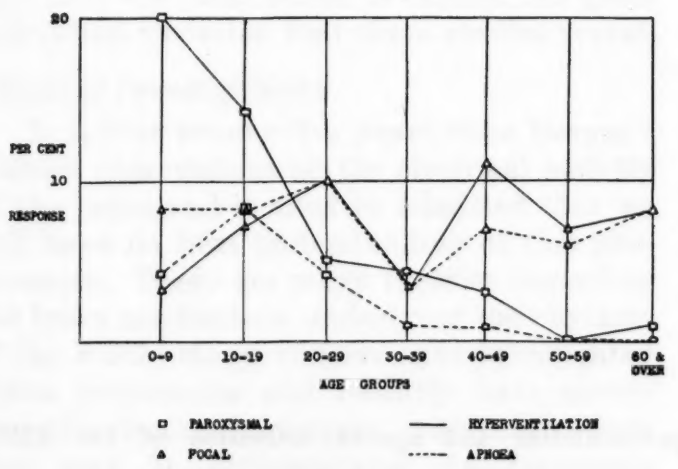

Fig. 7

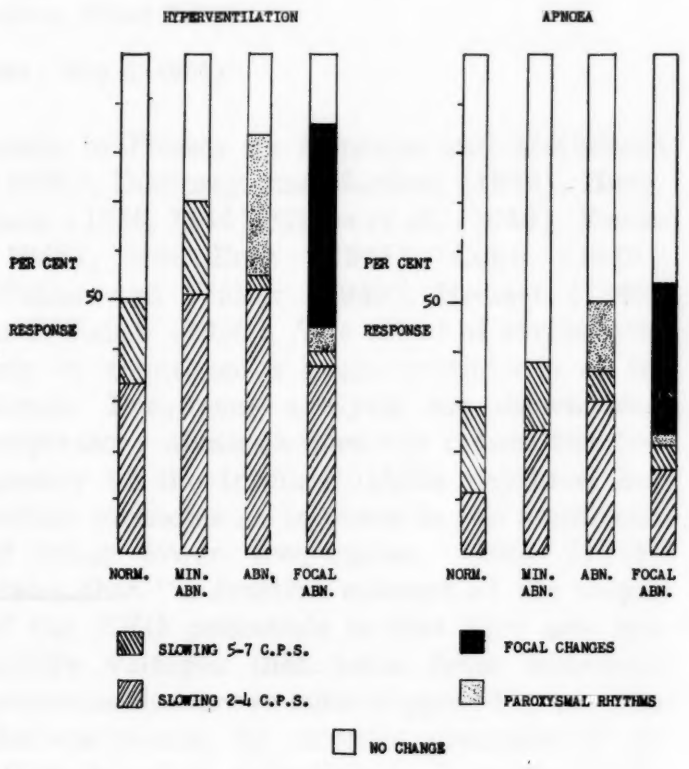

Fig. 8

SUMMARY

One thousand consecutive patients during routine electroencephalography were studied whenever possible by activation with hyperventilation followed by voluntary apnoea. The slowing of both hyperventilation and apnoea was inversely related to age and rarely by itself was considered a pathologic finding. Focal and paroxysmal dysrhythmias were elicited on both procedures and at times on apnoea alone. It is concluded that when the EEG diagnosis is not apparent from the previous record, apnoea is a simple, safe and quick procedure which in a small but significant percentage of cases may be used to advantage in the study of patients with suspected epilepsy, space-taking lesions, vascular and post-traumatic disorders.

REFERENCES

BICKERS, D. S. Electroencephalographic changes with hyperventilation followed by apnoea. *EEG Clin. Neurophysiol.*, **1953**, *5*: 129.

HULMBERG, C. The electroencephalogram during hypoxia and hyperventilation. *EEG Clin. Neurophysiol.*, **1953**, *5*: 371-376.

LLOYD-SMITH, D. L. The electroencephalogram during hyperventilation followed by apnoea. *EEG Clin. Neurophysiol.*, **1950**, *2*: 289-296.

Reference: SILVERMAN, DANIEL. A comparison of hyperventilation and apnoea activation of the EEG. *EEG Clin. Neurophysiol.*, **1956**, *8*: 41-48.

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SLOW WAVE PRODUCTION IN THE EEG, WITH REFERENCE TO HYPERPNOEA, CARBON DIOXIDE AND AUTONOMIC BALANCE

J. K. W. MORRICE, M.D.
Kingseat Hospital, Aberdeen, Great Britain

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INTRODUCTION

It is tempting to be critical of the contribution of electrophysiology to clinical psychiatry and to medicine generally. Nevertheless, I feel sure that electroencephalography, providing as it does now a valuable method of investigation, holds out the promise of a fuller understanding of cerebral function and disorder. To gain this reward, electroencephalography requires to elaborate new techniques and understand more intimately those which it now employs. The studies here described constitute a step along this road.

Slow waves and particularly delta waves (i.e. below 4 c/sec.) are probably most commonly withnessed in the EEG laboratory due to voluntary hyperpnoea. I have concerned myself therefore with the factors governing hyperpnoea and with the role of carbon dioxide in the CNS.

It is true to say that hyperpnoea has been accepted uncritically as a routine test in electroencephalography. Certain factors that govern the EEG response to overbreathing are known, but it is not generally realised that they are insufficient to explain the gross individual variation that these studies reveal.

Previous Investigations.

It is over twenty-five years since Berger's pioneer observations on the electrical activity of the brain and it must be admitted that we still have no firm understanding of this phenomenon. There are many theories regarding the brain mechanisms underlying the rhythms of the EEG. Many workers have investigated alpha frequencies and recently have shown that this rhythm is complex, with components that may be differentiated by frequency analysis and by means of their different reactions to stimuli. *Inter alia,* reference may be made to Dusser de Barenne and McCulloch (1938), Dempsey and Morison (1942), Hoagland (1936, 1944), Gibbs *et al.* (1940), Eccles (1945), McCulloch (1947), Cohn (1948), Walter and Walter (1949), Bremer (1949) and Walter (1950). The effect of overbreathing on spontaneous brain rhythms is of interest. Frequency analysis has shown that respiratory alkalosis does not reduce the frequency of the intrinsic alpha rhythms, but rather promotes an increase in the amplitude of other lower frequencies. Cohn (1949) states that "a fruitful concept of the origin of the EEG potentials is that they are primarily voltages that arise from metabolic processes that are in turn triggered by autochthonous means, by enzymic processes or by afferent action potentials". Darrow (1946) suggests that EEG frequencies represent a mechanism of mutual cortical-subcortical regulation which may involve activity of the autonomic nervous system.

Delta Rhythms.

Delta activity can appear in any part of the brain. It is usually said that its presence signifies depressed cortical function and the lower the frequency the greater the disturbance of function. Delta rhythms can arise from many and various causes and it would be an unrewarding exercise to catalogue them. There is yet no final mechanism which is the ultimate explanation of these waves.

It may be suggested that factors which interfere with the oxidative processes of the cerebrum tend to produce slow activity in the EEG. In normal adults, delta appears during hypoglycaemia, alkalosis, anoxia, deep sleep and anaesthesia. Such delta rhythm is usually large, diffuse and symmetrical. However, there is no evidence that the delta activity of

infancy, which is often asymmetrical, depends on a fundamental difference between the oxidative processes of the brain in infants and adults.

Several investigators, including Drooglever-Fortuyn and Jasper (1947), have shown that in animals stimulation of midline thalamic nuclei at a frequency of 3/sec. or so produces diffuse cortical discharges of delta type. It is probable that bilaterally synchronous delta in man arises similarly from midline nuclei, but it is important to distinguish between such activity and polyrhythmic asynchronous delta which may appear for different reasons and from a different source.

Various suggestions have been made regarding the significance of delta activity; for example, Walter (1938, 1950) has suggested that delta waves have a protective function when normal cortical activity is disturbed. He points out that such a mechanism for "failure to safety" is an essential device in the complex workings of the brain.

Delta waves are commonly induced in the EEG laboratory by asking the subject to overbreathe. In many cases overbreathing does not alter the EEG but, if it does, the commonest response is slowing. No definite or constant relationship has yet been established between any factor or group of factors and the appearance of delta waves on hyperpnoea. The ease with which these rhythms appear can be related to some extent to the following factors: age, rate and depth of ventilation, posture, oxygen content of the atmosphere, blood sugar and hydrogen ion concentration of the blood. One now offers the addition of a seventh factor, the "inherent stability" of the subject. Study of previous work suggests (Liberson and Strauss 1941; Williams 1941; Hill and Watterson 1942; Jewesbury 1952) that there is some intrinsic quality in an individual which determines his response to overbreathing and may outweigh the effect of the factors already known. As was shown by Mills (1946), hyperpnoea itself has a complicated effect on the cardiovascular and nervous systems and it may seem scarcely surprising that there is wide individual variation. On the other hand, it has been found (Engle *et al.* 1946) that the significant changes in blood pH and carbon dioxide content resulting from overbreathing take place during the first minute and seem to be of much the same order in everyone; yet the effect of overbreathing varies greatly from person to person.

There is general agreement that the delta response to hyperpnoea results from acapnia but there are three different theories regarding the more immediate mechanism. None of them, however, seeks to explain the gross individual variation noted above.

Theories.

1. The Hypocapnia Theory of Gibbs and his co-workers rules that the delta response is attributable to inadequate cerebral vasoconstriction. They say that vasoconstriction is the normal compensatory response to acapnia.

2. Davis and Wallace and their supporters have formulated the Hypoxia Theory which attributes the delta response to cerebral anaemia due to vasoconstriction. This results in deprivation of oxygen and glucose on which cerebral metabolism depends.

3. What might be termed the Cholinergic Theory of Darrow and his co-workers states that hyperpnoea causes reduction in the cholinergic activity of the cerebrovascular nerve supply which results in excessive local constriction and gives rise to abnormality in the EEG.

The experimental work which fathered these theories is of interest, but it is too extensive to be discussed here (Lennox *et al.* 1938; Gibbs *et al.* 1942; Kety and Schmidt 1946 and 1948; Davis and Wallace 1942; Darrow *et al.* 1944; Barnes and Amoroso 1946). In any event, despite the fact that some investigators (e.g. Schmidt 1944; Lloyd Smith 1950) would deny the importance of carbon dioxide in the production of delta waves and would continue the controversy, hypoxia versus hypocapnia, I believe that the problem has been sufficiently resolved to allow a working hypothesis to be formulated; this is due largely to the work of Darrow

(1945, 1946) and Hoagland (1946) and their co-workers.

It is possible that brain frequencies in resting subjects are proportional to cerebral respiration or the speed of certain chemical steps in this respiration. In particular, it may be suggested that carbon dioxide as an acid metabolite produced by cellular respiration is an important agent in firing the cell. Its production in the cell is a direct determinant of the cell's recovery from the refractory phase. Thus, the more carbon dioxide produced, the more rapid the recovery and hence the faster the frequency of firing of the cell. On the other hand, it is known that oxygen tension can be considerably reduced without modifying cerebral respiration. A critical limit is present, however, at which cellular respiration and therefore carbon dioxide production is affected.

There is thus little meaning to the controversy, hypocapnia versus hypoxia, in relation to the dynamics of brainwaves. Carbon dioxide is produced at a rate proportional to the respiration of the cells which itself depends on oxygen. It can therefore be said that theories 1 and 2 are complementary and are merely different facets of the truth.

It is tempting to speculate on the close connection between cerebral metabolism and electrical activity. In particular, the role played by carbon dioxide in the Krebs "tricarboxylic acid cycle" seems to offer scope for further investigation. It is possible, if highly speculative, that change in carbon dioxide tension alters the rate and direction of the cycle and may even provide an additional theory to explain the effect of hyperpnoea on the EEG.

Carbon Dioxide.

Carbon dioxide is a normal metabolite of living tissue. Its actions in animals and humans have been studied since the early 19th century. Its effects on respiration and circulation have been ascertained generally. Its effects on the central nervous system, however, are poorly understood despite recent intensive investigation.

The literature regarding the action of carbon dioxide on the central nervous system is surprisingly extensive, and the path that leads from the discovery by Loevenhart, Lorenz and Waters (1929) that 30 per cent to 45 per cent carbon dioxide makes catatonic patients respond with mental clarity for short periods, to the recent introduction by Meduna of carbon dioxide inhalation treatment for psychoneurotics, is somewhat tortuous and perplexing. Meduna (1950) points out that inhalation of high concentrations of carbon dioxide produces a temporary alteration of almost every nervous activity. So we see various motor and sensory phenomena and characteristic changes in the function of the vegetative nervous system. He quotes previous work by Gibbs, Williams and Gibbs (1940) whose administration of 5 and 10 per cent carbon dioxide caused increase in frequency and lowering of voltage of brain rhythm. According to Meduna, however, 30 per cent carbon dioxide causes slow, 3 to 4/sec., high voltage activity to appear usually about the 18th respiration. This activity continues for 20 sec. or so beyond the termination of treatment when it slowly reverts to normal.

It may be said then that carbon dioxide administration or excess, as well as carbon dioxide lack, can produce delta activity.

Occasionally the actions ascribed to carbon dioxide seem puzzling and even contradictory. Hill and Flack (1908) showed that in cats and dogs 10 to 25 per cent carbon dioxide gave rise to vagal and vasomotor stimulation; more than 25 per cent resulted in depression of cerebral activity or narcosis. Leake and Waters (1929) reported that, in addition to the general anaesthetic properties of carbon dioxide, muscular twitches and convulsions occur. On the other hand, Lennox and Cobb (1928) found that high concentrations of carbon dioxide stopped the convulsions of epileptics; and Lennox and others noted that carbon dioxide tended to abolish the spike and wave complex of petit mal subjects. McQuarrie and Ziegler (1938) reported that in dogs 15 to 20 per cent carbon dioxide inhibited insulin-induced convulsions. Gellhorn and Yesinick (1941) discovered that in

cats fits produced by Metrazol, picrotoxin and other agents were stopped by inhalation of 15 per cent carbon dioxide; but not if the carotid sinus was denervated bilaterally and the vagi cut. Pollock (1948) showed that in cats carbon dioxide antagonised convulsions induced by electrically stimulating the cortex. Stein, Pollock and Gyarfas (1949) demonstrated that electrically induced seizures in rhesus macacus and man are antagonised by carbon dioxide.

The carbon dioxide effects just categorised are not clear-cut, but this is possibly due to the varying percentages of the gas used by different workers. It has been suggested that convulsive agents can be divided into those whose action is enhanced by carbon dioxide and those antagonised by it. Pollock states that seizures synergised by carbon dioxide usually start in the hindbrain, while seizures antagonised by carbon dioxide start in the forebrain.

Recent work by Gellhorn (1953a) on the action of 10 per cent (''low'') carbon dioxide and 30 to 40 per cent (''high'') carbon dioxide on the hypothalamus and cortex of lightly anaesthetised cats is of much interest. He demonstrates what our survey of previous findings has implied, namely, a fundamental difference between low and high concentrations of carbon dioxide. He shows that the activity of the cerebral cortex depends on two different systems at least; that low carbon dioxide specifically increases the responsiveness of the hypothalamic-cortical system, while high carbon dioxide reduces and finally abolishes its reactivity; on the other hand the reactivity of specific cortical projection areas is diminished with low carbon dioxide inhalation and unimpaired by high carbon dioxide. Gellhorn (1953b) also discusses the therapeutic implications of his findings.

A Working Hypothesis.

It is accepted that resting brain rhythms depend on the chemical events occurring continuously within the brain cells. It is a reasonable if tentative hypothesis then that delta rhythms result from some upset in the normal respiration of the cells. It may be said in fact that delta activity may result from disturbance of the oxidative metabolism of neurones and particularly the oxidation of glucose. Oxygen and glucose are the working materials of brain cells and their importance has been demonstrated by their ability, when their level in the blood is raised, to prevent the appearance of slow rhythms.

However, delta activity and the oxidative metabolism of the cells are probably not directly related. Electrical rhythms are dependent on the state of the cell membranes and they in turn on the oxidative processes within the cells. Herein, carbon dioxide plays a fundamental role, although much controversy and ignorance still exist regarding its effects and regarding the detailed bio-electrics of brain cells. Nevertheless, the evidence suggests that carbon dioxide, produced normally by cellular metabolism, is the controlling factor in neurone excitability and in resting brain rhythms. It seems likely, therefore, that it is the alteration in carbon dioxide tension in the neuronal atmosphere produced by hyperpnoea or carbon dioxide administration that causes instability of the EEG and the appearance of slow waves.

The action and interaction of cell populations at different brain levels and particularly the relationship between cortex and diencephalon in the production of slowing in the EEG; the part played by the autonomic nervous system in homeostasis; and the nature of the individual variation in hyperpnoea response — these matters require elucidation.

MATERIAL AND METHODS

Electroencephalograms were recorded at first on a 6-channel and later on an 8-channel Ediswan. A wave-analyser was not generally in use and the records were examined by visual methods. Some use was made of an alpha-band filter. Subjects were drawn from hospital medical and nursing staff and from patients.

The experimental problem was approached from two directions. Firstly, studies were made in voluntary hyperpnoea and secondly in carbon dioxide administration — that is, from the point of view of tissue metabolism,

carbon dioxide lack and carbon dioxide excess. Thirdly, as it became clear that autonomic balance was a factor demanding investigation, tests of this function were made.

Hyperpnoea Experiments.

The procedure adopted was the one that seemed most straightforward and foolproof. It was decided to measure the amount of carbon dioxide expired during hyperpnoea in a standard situation and attempt to correlate this with the appearance of slow activity in the EEG. It may be noted here that a simple method of evaluating the intensity of hyperpnoea by estimating alveolar carbon dioxide content has been described by Asmussen and Buchthal (1949) and that Blinn and Noell (1949) have evolved a method of continuous measurement of alveolar carbon dioxide tension.

The subject reclined on the examination couch and electrodes were applied to the scalp in a standard placement. A nose clip was used and the subject breathed through the mouth atmospheric air via in-let and out-let valves. The expired air was collected via rubber-tubing in a large rubber bag fashioned for this purpose. The bag, having a capacity of 500 litres, was made large enough to accommodate the expired air without causing significant back-pressure which might well have embarrassed the subject's breathing (see fig. 1). Each subject was encouraged to breathe deeply, moderately quickly and regularly, but it did not always prove possible to secure full co-operation. The air collected in the bag was sampled by means of a syringe and the percentage of carbon dioxide was estimated. The volume of air expired was measured by drawing the air in the bag through a meter by means of an electric pump.

Samples of blood were taken from the subject during the procedure. The first was taken before the commencement of overbreathing; the second at the appearance in the EEG of definite slow activity. If no gross slowing occurred, the second sample was taken after hyperpnoea had been in progress for 3 min. Blood was taken from an antecubital vein and estimated for plasma carbon dioxide and carbon dioxide combining-power. Capillary blood from the ear lobe gave a measure of blood glucose.

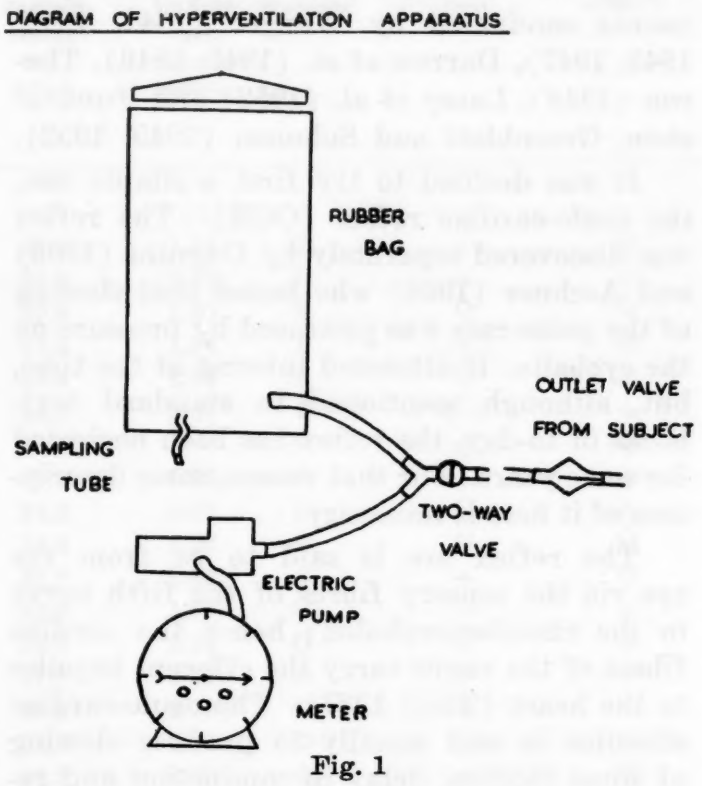


Fig. 1

It is realised, of course, that chemical estimations from peripheral blood samples cannot be said to mirror the events occurring in the cerebral circulation. However, in the absence of a simple and dependable method of sampling cerebral blood, this reservation was accepted.

Carbon Dioxide Experiments.

The methods used are described in the account of individual experiments. The apparatus for delivering carbon dioxide to the subject was that normally used in Meduna's inhalation therapy, namely 30 per cent carbon dioxide and 70 per cent oxygen delivered from a cylinder by flowmeter and anaesthetic mask with breathing-bag.

Where an electrocardiogram (EKG) was simultaneously recorded with the EEG, lead 1 was used.

Autonomic Function Experiments.

Much attention has recently been given to the autonomic nervous system, but survey of

the literature has revealed no test of autonomic function that is either simple or completely satisfactory. In a search for such a test, one considered particularly the experiments conducted by Wenger (1941, 1942, 1943, 1947), Darrow *et al.* (1945, 1946), Theron (1948), Lacey *et al.* (1952) and Funkenstein, Greenblatt and Solomon (1949, 1952).

It was decided to try first a simple test, the oculo-cardiac reflex (OCR). The reflex was discovered separately by Dagnini (1908) and Aschner (1908) who found that slowing of the pulse-rate was produced by pressure on the eyeballs. It attracted interest at the time, but, although mentioned in standard textbooks of to-day, the reflex has been neglected for some years. For that reason, some description of it here is necessary.

The reflex arc is said to be from the eye via the sensory fibres of the fifth nerve to the rhombencephalon; hence the cardiac fibres of the vagus carry the efferent impulse to the heart (Tinel 1937). The oculo-cardiac stimulus is said usually to produce slowing of sinus rhythm, delay in conduction and reduction in force of the heart beat (Schwob *et al.* 1936). In some subjects ocular pressure produces no change or, rarely, an increase in rate (paradoxical reflex).

It is considered that, in the absence of any lesion affecting the reflex arc and provided the heart is normal, the OCR may be used to assess the excitability of the vagus. The conclusions drawn cannot, in principle, be applied to the entire parasympathetic system; nevertheless, it seems true that in many cases a pronounced OCR is a sign of hyperexcitability of the vagus, whereas a "paradoxical reflex" indicates sympathetic predominance (Tinel 1937). I felt, therefore, that this simple test might provide a means of differentiating vagotonic from sympathicotonic subjects or, at least, provide an index on the scale of autonomic balance.

A further test was given in section IV. This is the test used by Funkenstein *et al.* (1949, 1952) which depends essentially on the reaction of systolic blood pressure to Epinephrine and Mecholyl. The authors have described their methods and technique fully and they were followed almost exactly by the present investigator.

On successive days, injections of Epinephrine and Mecholyl (i.e. adrenergic and cholinergic drugs) were given to selected patients. The drugs were injected at least 2½ hours after the last meal with the patient in bed. As far as possible the patient was at ease and the blood pressure basal. It sometimes took an hour's lying at rest to achieve a basal reading. Epinephrine, 0.05 mg. in 0.5 ml. water, was given intravenously. Systolic blood pressure was noted every 15 sec. after the injection until it returned to the pre-injection level and remained there 5 min. Mecholyl, 10 mg. in 2 ml. of water, was given intramuscularly and systolic blood pressure was followed every 30 sec. for 10 min. and then every minute until a total of 24 min. had elapsed.

In some cases, the pulse rate was also followed and in every case other physiological and psychological reactions were observed, e.g. flushing, pallor, anxiety.

Funkenstein and his co-workers described seven characteristic patterns of blood pressure response to the drugs and they concluded that "in a given individual the pattern of autonomic response represents something quite fundamental". They also correlated the patterns of autonomic response with the conventional clinical diagnostic groups of their subjects and found the correlation striking. In the light of these findings, it was felt that this test would be valuable in the investigation of autonomic reactions.

RESULTS

I. HYPERPNOEA

The following set of experiments comprises an investigation of hyperpnoea with reference to those factors of importance that are known but thought to be insufficiently understood.

(*a*) *Normal Subjects.*

Twenty-seven subjects were examined by the method already described and the results are shown in table I.

TABLE I

HYPERVENTILATION RESULTS IN NORMAL SUBJECTS

Subject	Plasma CO_2 (ml. per cent.)		CO_2 Combining Pwr. (ml. per cent.)		Blood Glucose (mgm. per cent.)		Vol. Expired (litres per min.)	CO_2 Expired (gm. per sq. metre)	Slowing Response	Consciousness	Paraesthesia
	R.	H.	R.	H.	R.	H.					
1.	64	60	64	64	81	87	35.6	1.05	D	+	O
2.	70	66	70	70	99	110	37.5	2.35	D	+	+
3.	59	57	60	60	75	81	30.9	1.80	d	O	O
4.	53	42	58	58	93	93	27.4	1.94	d	+	+
5.	62	52	66	64	52	81	36.4	2.38	d	O	+
6.	60	52	62	60	70	65	43.5	2.37	d	++	+
7.	60	53	60	59	93	81	—	—	D	+	+
8.	65	55	65	63	81	70	38.0	1.59	d	+	+
9.	66	62	68	66	97	104	24.2	2.01	O	O	+
10.	55	52	62	64	81	110	16.6	1.27	O	O	O
11.	61	57	66	63	93	93	20.7	1.31	d	+	O
12.	58	53	60	58	81	93	22.2	1.62	O	O	+
13.	61	60	68	68	81	70	20.0	2.06	O	+	+
14.	62	57	65	67	58	52	27.5	1.51	O	O	O
15.	67	62	68	68	46	58	25.8	2.00	O	+	+
16.	65	62	67	65	64	70	58.2	3.00	D	+	++
17.	62	57	64	64	58	58	24.3	2.09	d	+	O
18.	65	59	66	64	93	87	34.4	1.53	O	+	+
19.	63	61	63	64	70	75	23.2	1.75	O	+	O
20.	57	55	60	63	89	95	19.2	1.52	O	O	O
21.	56	53	62	61	70	93	38.3	1.57	D	+	++
22.	68	61	69	67	64	93	71.8	4.15	D	++	++
23.	68	61	69	67	70	58	31.2	1.69	O	+	+
24.	58	39	61	54	81	75	42.8	2.39	D	O	+
25.	55	46	62	54	75	75	50.4	2.94	d	O	+
26.	67	59	71	70	109	104	92.2	4.73	d	+	+
27.	62	55	66	64	86	94	72.6	5.19	D	O	++

R. = Resting State; H. = After Hyperventilation.

Examination of the EEG during hyperpnoea revealed three types of response which have been named D, d and O. In group D, the EEG showed definite high-voltage slow waves within delta range. Group d showed definite slow waves also, but not within delta range. Group O showed either no slow waves or only a minimal slowing response. Eight subjects fell into group D, 9 into d and 10 into O.

In this series each subject's height and weight were determined and his body surface-area was calculated using the formula of Du Bois. It was possible then to estimate the carbon dioxide expired in grams per square metre of body surface, thus giving a more comparable measurement of subjects.

Table I shows a wide range of values, despite the standard experimental situation, for the changes in blood chemistry, the volume of air expired and the amount of carbon dioxide expired. Mean values for the three groups D, d and O, were calculated and are shown in table II.

These figures show (from the point of view of the three groups described) that delta

waves on hyperpnoea are produced by the subjects who breathe out most air the most quickly. With regard to the rate of expiration, carbon dioxide expired and drop in circulating carbon dioxide, there appears a definite trend among the three groups and a marked difference between those subjects who show slow waves and those who do not. The small differences between the blood glucose levels of the three groups are insignificant and can in no way affect the trends noted above. On statistical analysis, there is a highly significant difference between groups D and O in respect of air expired ($P < 0.001$). The other two measurements (carbon dioxide expired and drop in plasma carbon dioxide) show differences between the groups that are not statistically significant.

TABLE II

MEAN VALUES IN HYPERVENTILATION GROUPS

Group	Air Expired (Litres/ min.)	CO_2 Expired (gm./sq. metre)	Drop in Plasma CO_2 (ml. %)	Blood Glucose (mgm. %)
D	51 ± 6.	2.8 ± 0.5	6.8 ± 1.9	79.7
d	40 ± 7.	2.4 ± 0.3	7.4 ± 1.0	78.4
O	24 ± 2.	1.7 ± 0.1	4.0 ± 0.6	76.6

It might appear then, at first glance, that the occurrence of delta waves depends on the rate of expiration and the amount of carbon dioxide breathed off. That those are important factors there can be no doubt. Nevertheless, examination of table I will reveal (and this point will be further illustrated) that these factors alone cannot be held responsible for the appearance of delta waves, even when the other known factors affecting the overbreathing response are under experimental control. For example, subjects 1 and 18 in table I have comparable blood chemistry values and rates of expiration; indeed, subject 18 expires considerably more carbon dioxide than subject 1. Nevertheless, it is subject 1 who produces delta waves whereas subject 18 shows no significant slowing.

At the end of the period of hyperpnoea, the 27 subjects were asked to describe any unusual sensations they had experienced. If no positive information was given, leading questions were asked about disturbance of awareness and paraesthesiae. Alterations of consciousness and paraesthesiae were measured, therefore, by the subject himself and were purely subjective except when there was obvious physical change to be seen or when the subject did not respond normally to questions or commands. It was found that these disturbances could be divided into three categories according to the degree of change experienced. The symbols used for the groups are ++, + and O.

Consciousness: Group ++ subjects showed marked change, described as faintness, remoteness and dizziness. Group + subjects noticed a change of awareness but only of slight degree. Group O subjects showed no change.

Paraesthesia: Group ++ subjects showed marked change, described as tingling, stiffness or actual pain in limbs, trunk or face. In many of this group physical signs of tetany were readily apparent. Group + subjects noticed a change of the same quality but of much less severity or extent. Group O noticed no change.

Table I shows these factors, as they are related to blood changes, respiratory effort and EEG slowing, for each individual. Table III demonstrates their occurrence in the groups divided as to slowing response.

TABLE III

DISTURBANCES OF CONSCIOUSNESS AND SENSATION IN HYPERVENTILATION GROUPS

Group	No. of Subjects	No. showing Disturbances of Consciousness	No. showing Paraesthesiae
D	8	6 (75%)	7 (88%)
d	9	6 (67%)	6 (67%)
O	10	5 (50%)	6 (60%)

These tables reveal that although delta waves in this series are nearly always accompanied by disturbance of consciousness, the converse is not true. Disturbance of conscious-

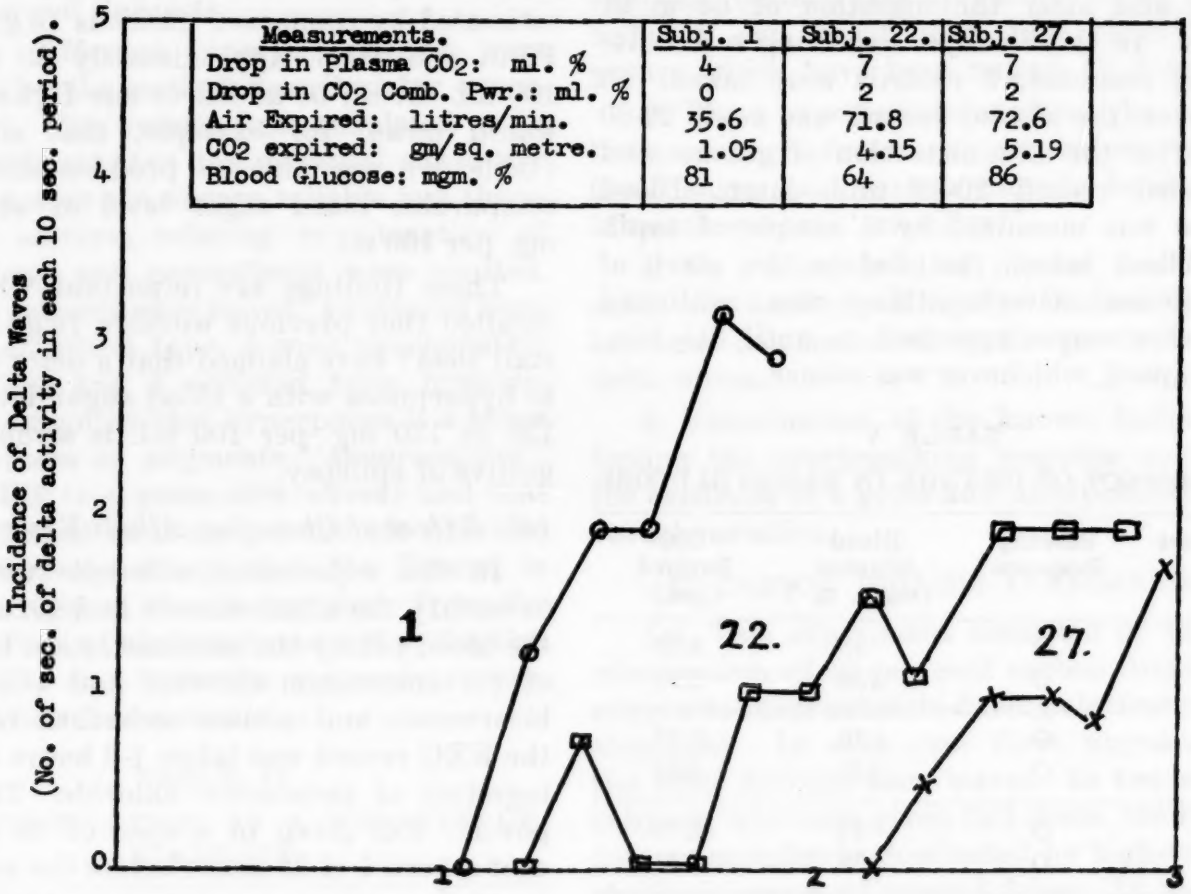
ness can be present indeed without any apparent slowing whatever. It is also noteworthy that disturbance of consciousness and paraesthesia do not go necessarily hand in hand and one's impression is that paraesthesia depends to a greater extent than disturbance of consciousness on the amount of air or carbon dioxide expired. In any event it can be said that vigorous hyperpnoea, whether or not in results in disturbance of consciousness, tends to produce paraesthesia. This is evidence in support of the theory that these two effects of hyperpnoea are not interdependent; rather, one depends on cerebral circulatory changes and the other on peripheral.

At this stage it is important to note that even within the three groups, D, d and O, there is variation between individuals that is difficult to explain by the action of factors that are known. For example, in group D subjects 1, 22 and 27 (table I) show wide variation in the factors measured, although all three produce high voltage delta (see table IV).

These findings lead to the proposition that, although the factors accepted as affecting the overbreathing response in the EEG (namely, age, ventilation, posture, oxygen content, blood sugar and blood pH) are, broadly speaking, sufficient to explain the differences that occur between the three groups, designated D, d and O, they do not satisfactorily explain the differences between individuals within these groups.

TABLE IV - INDIVIDUAL VARIATION WITHIN GROUP D.

Measurements.	Subj. 1	Subj. 22.	Subj. 27.
Drop in Plasma CO_2: ml. %	4	7	7
Drop in CO_2 Comb. Pwr.: ml. %	0	2	2
Air Expired: litres/min.	35.6	71.8	72.6
CO_2 expired: gm/sq. metre.	1.05	4.15	5.19
Blood Glucose: mgm. %	81	64	86



(b) Hyperpnoea repeated.

In three different subjects the overbreathing test was repeated on more than one occasion. Whereas the results detailed in table I demonstrate the different amounts of carbon dioxide different subject expire to achieve

slowing of the EEG, the present experiment reveals that differences occur in one individual at different times. In the latter case, however, an individual's figures approximate fairly closely and the variation is explicable (or so it seems) by what we know of the effect of changes in blood sugar and alkali reserve on the EEG in hyperpnoea.

(*c*) *Effect of change in blood sugar.*

In this experiment, the EEG response to overbreathing was examined in 7 subjects before and after the ingestion of 60 g. of glucose. In those subjects showing a definite slowing response, 3 records were taken. In each case, the second record was made 20-30 min. after the administration of glucose and the third record 20-30 min. later. Blood glucose was measured by a sample of capillary blood taken just before the start of hyperpnoea. Overbreathing was continued until slow waves appeared or until 3½ min. had elapsed, whichever was sooner.

TABLE V

THE EFFECT OF CHANGE IN BLOOD GLUCOSE

Subject	Slowing Response	Blood Glucose (mgm. %)	CO_2 Expired (gm.)
1.	O	93	3.70
	O	139	3.50
2.	O	70	3.17
	O	151	3.35
3.	O	93	2.79
	O	139	3.18
	d	72	3.06
4.	d	93	3.48
	d	133	3.59
	D	99	2.15
5.	D	122	3.09
	D	93	1.21
	D	81	1.05
6.	D	93	2.08
	D	128	3.11
	D	75	2.40
7.	D	139	7.07
	D	104	4.73

The results of this small series are shown in table V. They demonstrate convincingly that the higher the blood sugar level, the more carbon dioxide must be expired to produce definite delta in the EEG.

It is worthwhile noting that the slowing response occurred in some subjects at blood glucose levels about 120 or 130 mg. per 100 ml. Moreover, it must be remembered that these measurements are of true blood glucose (method of King *et al.* 1937) and, if they are to be compared with blood sugar levels as estimated by commoner methods (e.g. that of Folin and Wu), approximately 20 mg. per 100 ml. should be added to our figures. This would mean, for example, that subject 7 (table V) was able to produce delta at a comparable blood sugar level of about 160 mg. per 100 ml.

These findings are important when it is recalled that previous workers (e.g. Heppenstall 1944) have claimed that a delta response to hyperpnoea with a blood sugar level above 120 or 130 mg. per 100 ml. is strongly suggestive of epilepsy.

(*d*) *Effect of Changing Alkali Reserve.*

In this experiment, attempts were made to modify the alkali reserve and consequently the blood pH by the administration by mouth of (i) ammonium chloride and (ii) sodium bicarbonate and calcium carbonate. In general the EEG record was taken 1-2 hours after the ingestion of ammonium chloride. The alkali powder was given in a dose of 60 g. taken over a period of 36 hours before the recording.

The results are inconclusive. Although the administration of acid or alkali by mouth caused in almost all subjects a considerable alteration in alkali reserve, a significant accompanying alteration in the overbreathing response of the EEG did not occur. This failure of emergence of clear-cut results may be due in some part to the effect of change of other factors, e.g. blood glucose.

Acid Administration.

Of 5 subjects, one showed a facilitation in slowing response, 3 were unchanged and one showed inhibition.

Alkali Administration.

Of 5 subjects, 2 showed facilitation in slowing response, 2 were unchanged and one was inhibited.

These results neither support nor disprove the theory that a rise in alkali reserve facilitates the slowing response to hyperpnoea. It may be felt, however, that the comparative lack of response of the EEG to induced alkalaemia suggests that the delta response may not depend on change in pH of the blood.

(*e*) *Abnormal Subjects.*

Three different types of patient were examined by the method described for experiment (*a*). The results were tabulated as in that experiment, but the patients' subjective sensations were not always reliable and therefore the sections relating to alteration of consciousness and paraesthesia were omitted. Thirteen patients were tested; 4 suffered from epilepsy of mixed type, 4 were psychopathic personalities and 5 suffered from hysteria.

If it is granted that hyperpnoea is a stress that produces or augments "abnormalities" in the EEG (e.g. gross slow waves) and that the air expired in litres per minute provides an index of the stress, then the figures in table VI support the theory that, from the point of view of electrophysiology, epileptics, psychopaths and hysterics are more susceptible to stress than normals.

TABLE VI

HYPERVENTILATION AS A MEASURE OF STABILITY

Subjects Showing D Response	Mean Vol. of Air Expired (litres per min.)
Normals	51.0
Hysterics	30.6
Psychopaths	24.0
Epileptics	18.8

This series is very small and by itself could not of course uphold a hypothesis. Moreover, because of the small numbers in the abnormal groups, their ranking is not statistically valid. Nevertheless, the series serves to confirm and augment the general impression that the delta response to hyperpnoea is greater in epileptics than in non-epileptics.

Conclusions.

These experimental findings may be stated shortly as follows:

1. Hyperpnoea is not the simple test that some investigators have thought it.

2. There is a range of EEG response to hyperpnoea from no slowing (or even exaggeration of fast frequencies) to high-voltage rhythmic delta waves appearing in all leads. Subjects can be divided into three main groups which have been named D, d and O.

3. These experiments confirm the importance of such factors as expiratory effort, blood sugar and carbon dioxide levels, and inherent cerebral "stability".

4. No critical level of plasma carbon dioxide nor amount of expired carbon dioxide has been demonstrated in the production of delta waves.

5. Examination of the known factors affecting the overbreathing response confirms the existence of a gross and unexplained individual variation.

II. CARBON DIOXIDE INHALATION

(*a*) This experiment consisted of the administration of 30 per cent carbon dioxide in oxygen to three subjects during electroencephalography. In each case there appeared in the EEG definite slow waves. In two of the subjects, who were given full doses, the record became completely dominated by high-voltage rhythmic waves of around 3/sec. In view of this striking effect further records were made and in addition blood samples were taken so that the chemical changes could be followed.

Four subjects were examined in this manner with the results shown in table VII. It will be seen that in no case did the administration of the gas mixture cause deficient oxygenation; indeed the reverse tended to occur. The EEG effects therefore cannot be ascribed to anoxaemia.

(*b*) Sixteen subjects were given carbon dioxide in the standard fashion described above and EEGs were simultaneously record-

ed. A remarkable similarity in the response of all cases was noted. Every subject produced large delta waves in the EEG and the changes followed much the same sequence.

TABLE VII

BLOOD CHEMISTRY CHANGES ON CARBON DIOXIDE INHALATION

Subject	Blood Glucose (mgm. %)	Blood Oxygen (ml. %)	Plasma CO_2 (ml. %)	CO_2 Comb. Pwr. (ml. %)
1. Resting	64	16.1	60	66
At appearance of delta.	—	15.3	73	78
2. Resting	81	8.4	61	64
At appearance of delta.	—	14.2	69	69
3. Resting	70	12.5	62	67
1 min. after appearance of delta.	—	15.6	74	73
4. Resting	87	7.9	69	71
Delta Disappeared; Mask off 2 min.	—	7.9	69	72

Generally speaking, the alpha rhythm becomes much less evident when the subject begins to breathe the carbon dioxide mixture. Soon there appear frequencies in the theta range and then a rapid build-up in all leads to high-voltage bilaterally synchronous delta waves of 3 to 4 c/sec. (see fig. 2). These waves completely dominate the record. They appear usually in just over one minute after carbon dioxide administration is begun. When administration is stopped the delta waves gradually fade and the alpha rhythm becomes evident once more.

In 3 subjects use was made of an alpha-filter on one channel. The filtered record shows, in these 3 cases, that the alpha waves disappear or almost disappear when the administration of carbon dioxide is begun and they remain so until the delta rhythm dominates the record. Then the alpha returns. This cannot be seen in the ordinary tracing where alpha is not readily visible amidst the dominant high-voltage delta waves. It is possible, however, that this "return" of alpha frequency is in fact merely an indication by the filter of increased regularity of delta frequency with an asymmetrical waveform giving second or third harmonics. In any event, examination of the ordinary tracings shows that alpha may persist (although usually attenuated) after the administration of carbon dioxide has begun. In 14 records that are clearly readable with regard to alpha frequency (until the masking effect of delta), alpha disappears in 8 and persists in 6. It can be seen then that the relationship of alpha to delta is variable in this regard and not easily explained.

(*c*) An experiment was performed on 7 subjects to determine the effect of a raised blood sugar level on the delta waves produced by carbon dioxide. The first subject was given 60 g. glucose by mouth and the record taken one hour later. The other 6 subjects were given 30 g. glucose intravenously and the records taken 10 min. later. The recordings made after the administration of glucose were in every case compared with those taken with the subject in the resting state.

The results show that, even with a very large increase in blood glucose, slow waves produced by carbon dioxide inhalation are not inhibited to any significant extent. With regard to the persistence of alpha, 5 of the 7 subjects showed no change after the administration of glucose; in 2 the alpha persisted after glucose whereas before it had disappeared. In such a small series this cannot be said to be of any significance but such an "enhancing effect" of glucose on alpha frequencies recalls the work of Wyke (1952).

(*d*) EEG recordings with simultaneous electrocardiograms (EKG) were made along with carbon dioxide administration in each of 4 cases. The stimulus to record the EKG was the observation that, during the therapeutic administration of carbon dioxide to patients, pulse changes occurred varying with the different stages of response.

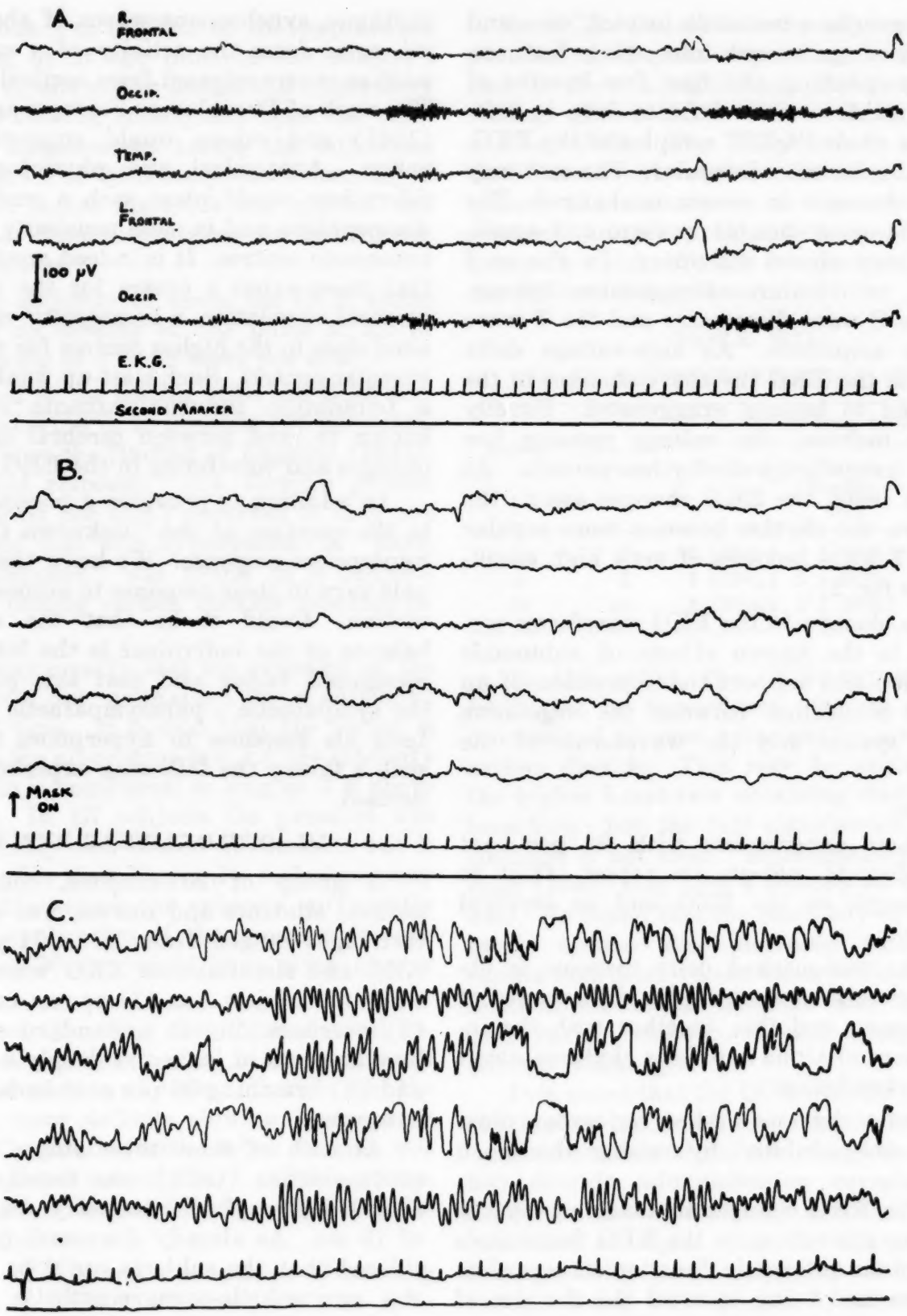


Fig. 2

The effect of CO_2 upon the EEG and EKG.

A: Resting period.
B: Inhalation of CO_2 begins.
C: Build-up of delta waves.

Two records were made in each case and these 8 tracings reveal interesting features. Generally speaking, the first few breaths of carbon dioxide cause a definite drop in voltage of the whole PQRST complex of the EKG. The rhythm becomes irregular. The rate may increase, decrease or remain unchanged. The P wave becomes variable in form and amplitude; it may almost disappear. In one or 2 tracings ventricular extrasystoles appear. Often the S wave disappears and the T wave drops in amplitude. As high-voltage delta appears in the EEG the above changes in the EKG tend to become exaggerated. Usually the rate increase, the voltage remains low and the irregularity of rhythm persists. As the delta fades, the EKG changes again; the rate slows, the rhythm becomes more regular and the T wave becomes of very high amplitude (see fig. 2).

These changes in the EKG waveforms correspond to the known effects of autonomic stimulation and support the impression of an intimate connection between the vegetative nervous system and the waveforms of the EEG.

Conclusions.

1. These experiments with 30 per cent carbon dioxide indicate its potent effect in this strength on the EEG and on cerebral function.

2. The well-marked delta response is obviously closely connected with disturbance of consciousness and this, together with the interrelations of alpha and delta rhythms, await further elucidation.

3. Delta rhythms evoked by carbon dioxide are not inhibited by raising the blood glucose.

4. The EKG changes that accompany the frequency alterations in the EEG focus one's attention on autonomic function in regard to the latter and bring to mind the theories of Darrow regarding the role of the autonomic nervous system in cerebral regulation.

5. The production of high-voltage delta waves on hyperpnoea and their appearance in a subject receiving 30 per cent carbon dioxide pose a question. Do these high-voltage, rhythmic, synchronous waves of about 3 per sec. arise from the activity of a subcortical midline centre released from cortical control ? The work of Droogleever-Fortuyn and Jasper (1947) and others would support such a notion. Anatomical and physiological considerations would place such a centre in the diencephalon and in close proximity to higher autonomic centres. It is indeed most probable that there exists a centre for the control of cerebral circulation, a homeostatic mechanism sited close to the higher centres for peripheral vascular control. Such a set-up would provide a foundation for the intimate connection known to exist between cerebral circulatory changes and waveforms in the EEG.

In addition it provides a possible answer to the question of the "unknown factor" in hyperpnoea response. We know that individuals vary in their response to autonomic stimulation. Could it be that the autonomic balance of the individual is the hitherto unrecognised factor and that this position on the sympathetic - parasympathetic range affects his response to hyperpnoea ? To test such a theory the following experiments were devised.

III. OCULO-CARDIAC REFLEX

A group of 20 subjects, composed of medical students and nurses, was examined; their ages ranged from 19 to 31 years. An EEG and simultaneous EKG were recorded while the subject was (1) at rest on a couch; (2) overbreathing at a standard rate of 28 breaths per min., taken as deeply as possible; and (3) breathing 30 per cent carbon dioxide in oxygen.

At each of these three stages the oculocardiac reflex (OCR) was tested, the stimulus being applied bilaterally for a period of 15 sec. As already discussed, it was considered that the subjects could be placed on the sympathetic-parasympathetic range of autonomic balance according to the amount of slowing produced.

During hyperpnoea the OCR was applied at the appearance of definite slow activity in the EEG or after 3 min. whichever was sooner. During carbon dioxide administration

the stimulus was applied at the appearance of slowing or at the limit of the subject's tolerance of this rather distasteful respiratory task. The slowing consequent upon the stimulus was measured by taking the difference in the number of QRS complexes occurring in the 10 sec. before the OCR was applied and the number occurring during the last 10 sec. of the stimulus.

In the majority of cases, the OCR either produced no slowing of the pulse at all or else a slowing of 1 to 12 beats per min.

Applied in the resting state the OCR produced no slowing in 10 subjects (50 per cent). This confirms the finding of Dagnini (1937). A "marked response" (i.e. slowing greater than 12 beats per min.) occurred in only one subject and that with hyperpnoea. A "paradoxical response" was found in 4 subjects but only during carbon dioxide administration.

This may signify that the pressure on the eyeballs was not maintained for a sufficient length of time. It is said that the reflex is subject to the all-or-none law, i.e. the intensity of stimulus is immaterial so long as it is above threshold. In all subjects the pressure was applied firmly and caused discomfort; but it seems possible that Dagnini's technique may fail to differentiate the subjects sufficiently well and application of the pressure for say a period of 30 sec. might have given clearer results.

It is worth noting that "paradoxical responses" occurred not at all in D group, even with the inhalation of carbon dioxide. On the contrary, more definite slowing in response to the O.C. stimulus with carbon dioxide was noticeable in 4 out of the 7 in this group. This suggests hyposensitivity of the sympathetic system.

Table VIII shows the number of slowing responses to OCR in the subjects who have been categorised according to their overbreathing responses. A difference is evident between the three groups D, d and O, which indicates that subjects who produce slowing in the EEG with overbreathing are much more prone to produce slowing of the heart-rate in response to the OCR. On statistical analysis, the proportions of subjects responding in groups D and O show a significant difference when resting ($P < 0.05$) and with hyperpnoea ($P < 0.05$). The difference is not quite significant with carbon dioxide; but this ignores the occurrence of "paradoxical responses" in group O and their absence in group D, which, if taken into account, renders the difference significant.

TABLE VIII

OCR IN HYPERVENTILATION GROUPS

Group	No. in Group	No. slowing to OCR		
		Resting	Hyper Ventilation	Carbon dioxide
D	7	6 (86%)	7 (100%)	4 (67%)
d	3	1 (33%)	2 (67%)	1 (33%)
O	10	3 (30%)	5 (50%)	1 (10%)

In this series, the OCR appears to be facilitated by hyperpnoea whereas its effect is impaired or even occasionally inverted by carbon dioxide. This may be explained by the higher heart-rate obtaining during overbreathing; but the full significance of these findings is not clear. Investigations of Gellhorn (1943) may have a bearing on this, however. He found that the reactivity of the autonomic system was increased with hypercapnia and more recent observations (quoted in Gellhorn 1953a) showed that 10-15 per cent carbon dioxide elicited sympathetico-adrenal discharges.

It is noted that the OCR inhibits the alpha rhythm but has no effect on delta.

Examination of the recordings during carbon dioxide administration reveals effects similar to those previously detailed; namely, inhibition of alpha with the appearance of theta activity and ultimately delta; these changes being accompanied by alterations in the voltage, rate and form of the electrocardiogram that signify autonomic effects.

An impression gained during the original overbreathing experiments was renewed during the course of these tests, namely, that the subjects who respond to hyperpnoea by

the production of slow waves in the EEG are those who show most slow activity in their resting records. Careful visual examination of the records in this series confirms such a tendency while showing that the rule does not always hold good. It is found that activity slower than alpha and obvious to visual inspection occurs in 100 per cent of group D, 67 per cent of group d, and 50 per cent of group O.

Conclusions.

At first sight it might appear that groups D and d, since they respond more readily to OCR, tend towards the parasympathetic end of the scale, whereas group O, which responds poorly to OCR, tends towards the sympathetic. However, Wilder's rule (1931) points out that attention must be paid to the resting or original vegetative state; the higher the degree of excitation of a vegetative organ the less its excitability in the same direction and the greater in the opposite direction. This would suggest then that groups D and d are, in fact, inclined towards the sympathetic and group O towards the parasympathetic poles. This is a more acceptable finding in the light of previous knowledge, for example the work of Darrow *et al.* and Wenger's belief that the more stable a person is the more the parasympathetic predominantes over the sympathetic.

Another explanation is possible, however. It may be that those subjects whose EEGs slow on hyperpnoea are more labile and respond more readily to autonomic stimuli than the more stable subjects whose EEGs show no slow activity. The response of these labile subjects may therefore appear "sympathetic" or "parasympathetic" according to the nature of the stimulus applied. It is also possible that labile subjects whose autonomic balance is more easily disturbed, are emotionally upset to a greater extent than the stable by the experimental situation and this results in sympathetic predominance.

Further experiments were therefore performed in an attempt to elucidate the matter.

IV. AUTONOMIC DRUGS

(*a*) Twenty-four subjects were examined by the methods of Funkenstein and his coworkers which have already been described. All the subjects were male, as it has been suggested that a sex difference exists in autonomic response (Igersheimer 1953). Ages ranged from 15 to 39 years. An arbitrary upper limit of 40 years was set because of the recognised inhibitory effect of advancing age on the slowing response of the EEG to overbreathing.

The experimental group was derived from 42 patients whose EEGs were recorded with particular reference to hyperpnoea. This was performed at a standard rate of 28 breaths per min. for 3 min., respiration being as deep as possible. As before, the overbreathing response was categorised D, d and O.

It proved impossible for various reasons to examine with autonomic drugs all 42 patients; some, for example, required active physical treatment before the completion of the experimental routine. Moreover, after a total of 12 in group O had been examined, further subjects in this group were neglected. Interest was mainly centred in those subjects showing a slowing response to overbreathing and it was disappointing to find only 15 such responses (D + d) in the 42 subjects examined.

In this series, group O constituted 64 per cent of the total, d 19 per cent and D 17 per cent. The subjects examined in the previous experiment fell into the 3 hyperpnoea groups as follows: O = 50 per cent, d = 15 per cent and D = 35 per cent. The discrepancy that exists between the two series can probably be explained by the age factor. The mean age in III was 24 years with only one subject over 30 years. In this series the mean was 28 years with 15 subjects over 30 years. This demonstrates that the slowing response to overbreathing is much rarer after the third decade.

Mean figures for the three hyperpnoea groups are shown in table IX. It will be noted that group D subjects are more susceptible to change in blood pressure and require longest for homeostasis with regard to both

Epinephrine and Mecholyl. The differences between group d and group O are not so marked. Analysis reveals that the differences between the groups are not statistically significant. If group d is left out of account, however, there is a significant difference between groups D and O with regard to time to homeostasis after Epinephrine ($t = 2.5$). It should also be recalled that fall of blood pressure after Mecholyl was followed for 24 min. only, at the end of which period many group D subjects had not achieved homeostasis. The mean time for this group, therefore, errs on the low side.

TABLE IX

REACTION TO AUTONOMIC DRUGS OF HYPERVENTILATION GROUPS: MEANS

Group	B.P. rise with Epinephrine (mm.hg.)	Time to Homeostasis (min.)	B.P. fall with Mecholyl (mm.hg.)	Time to Homeostasis (min.)
D	64.0	8.8	13.7	21.5
d	48.7	7.5	10.3	19.2
O	50.6	6.9	9.8	16.2
	S.E. of Difference			
D v d	± 9.1	± 1.3	± 3.5	± 3.7
D or d v O	± 7.9	± 1.1	± 3.0	± 3.2

The subjects were questioned regarding tremor, sweating, palpitation and anxiety, and notice was taken of flushing and pallor. All patients showed some of these changes. There was no significant difference in their incidence in the three groups. The majority of patients reacted to Epinephrine by marked pallor which passed off after a min. or 2 to be succeeded by flushing; palpitation and anxiety tended to appear also. Reactions to Mecholyl were generally much less evident, flushing being the commonest.

Other reactions of interest occurred. In some instances, neurotic subjects responded to Epinephrine with the very symptoms which had brought them into hospital. One patient reacted with a typical anxiety attack characterised by palpitation, restlessness, dyspnoea and apprehension. In this same individual, Mecholyl, given the next day, caused a general if temporary improvement of symptoms which he described thus: "I feel just the reverse of yesterday. The injection seems to have steadied me up and I feel much better, more like my old self." Such responses, one feels, provide evidence that a state of autonomic imbalance is not merely a theoretical concept but an actual condition present in at least some neurotics, and which can find symptomatic relief in appropriate autonomic stimulation.

The changes in pulse-rate which accompanied changes in blood-pressure were rather variable and there were no significant differences between the overbreathing groups in this respect. Most subjects, immediately on the injection of Epinephrine, reacted with an irregular, slower and sometimes faint pulse. Apart from this, change in blood-pressure was followed in the same direction by pulse-rate.

Seven varieties of systolic blood-pressure graphs are described by Funkenstein and his collaborators. In table X are shown the number of subjects in each hyperpnoea group that fall into each autonomic group. As far as possible one has recognised the criteria laid down by the original investigators but, as they themselves have remarked, some cases are not easily fitted into this scheme.

TABLE X

RELATIVE INCIDENCE OF SUBJECTS IN HYPERVENTILATION AND AUTONOMIC GROUPS

Hyperventilation Groups	Autonomic Groups						
	I	II	III	IV	V	VI	VII
D	1		1	1		3	
d			1	1	2	2	
O		1	8	2	1		

This table illustrates how subjects in groups D and d tend towards the higher autonomic categories, whereas group O subjects tend towards the middle and lower. Broadly speaking, this means that subjects

with slowing responses have a delayed homeostasis to autonomic stimulation, while subjects who do not slow establish homeostasis earlier. It is also true that subjects in the higher autonomic groups have an increased response to parasympathetic stimulation; but most of group D reacted well to both drugs and any tendency for a greater response to Mecholyl is slight.

Funkenstein and his co-workers have discussed at length the relations of diagnostic categories to autonomic groupings. Our material, when analysed in this way, showed no trends of significance. One noted, however, that, despite the frequently affirmed rigidity and unresponsiveness of schizophrenics (e.g. Rubin 1942), our patients in this diagnostic category proved responsive to both hyperpnoea and autonomic stimulation. The correlation of such responsiveness with a favourable prognosis (Meadow *et al.* 1953) raises a point of interest.

TABLE XI

EFFECT OF AUTONOMIC DRUGS ON HYPERVENTILATION GROUPS

Subject	Hyperventilation Groups		
	Without Drugs	After Epinephrine	After Mecholyl
R.C.	O	O	O
D.B.	d	D	D
A.F.	O	O	O
R.M.	O	d	O
R.H.	O	O	O
S.C.	O	d	O

(*b*) In an attempt to discover whether autonomic stimulation by drugs could cause a change in overbreathing response, 6 subjects were examined. They were patients whose normal response to hyperpnoea had already been determined. While the EEG was recorded, each subject was given Epinephrine 0.05 mg. intravenously and this was followed later (when blood pressure had returned to normal) by an intramuscular injection of 10 mg. of Mecholyl. No gross changes occurred in the EEG in any subject with the drugs alone, which therefore were followed, after appropriate intervals, by 3 min. overbreathing at the standard rate. The results of this experiment are shown in table XI. A convincing change in the hyperpnoea category occurred in only one subject.

The work of Greenblatt *et al.* (1947) is interesting in this connection. The experiments performed and quoted by these authors reveal that autonomic stimuli, whether sympathicomimetic (Epinephrine) or parasympathicomimetic (Mecholyl), cause changes that are much more marked in basal than in cortical recordings. It is possible, therefore, that the lack of response of my subjects was merely apparent and due to the conventional electrode placement.

Conclusions.

1. These experiments serve to confirm that subjects in group D are more labile than those in group O, and that they take longer to achieve homeostasis after autonomic stimulation. Although some of the results are not statistically significant (which is not surprising when one considers the many variables involved) the constant trend of differences between the groups is unmistakable.

2. No definite imbalance towards either the sympathetic or parasympathetic side has been demonstrated in any group of subjects. The tendency towards a parasympathetic response in subjects slowing on hyperpnoea, noted in the oculo-cardiac reflex experiments, has not been convincingly substantiated. Our results show in fact that the majority of such subjects are autonomically labile in either direction.

3. A correlation exists, therefore, between instability to hyperpnoea and instability to autonomic stimulation.

4. Consequently, it is probable that the hitherto unrecognised factor underlying individual variation in the response of the EEG to overbreathing is the inherent stability of the autonomic nervous system.

5. Tests of autonomic function and balance have been demonstrated with implications that extend beyond the boundaries of electrophysiology.

DISCUSSION

Hyperpnoea is a widely used test in electroencephalography. Until lately it has been usual to look upon it as a simple stress that tends to lay bare certain abnormalities in the EEG. These studies have shown that hyperpnoea has a complicated action and they underline the fact that its use as a routine test requires knowledge of the factors involved.

It was considered convenient to group overbreathing responses into three categories — D, d and O — according to the amount of slow activity present. Since there is a continuous range in overbreathing response, the three groups have somewhat arbitrary borders. Nevertheless, these investigations of the factors influencing the EEG response have validated the reality of the categories.

No critical level of plasma carbon dioxide in the occurrence of the delta response was demonstrated. This agrees with the findings of Blinn and Noell (1949). They measured alveolar carbon dioxide tension during hyperpnoea and found that the first appearance of slow wave activity in the EEG occurred over a wide range of tensions. In other words, as investigation of the various factors has shown, individual constitution overshadows the effect of respiratory effort and changes in blood chemistry.

The importance of carbon dioxide in cerebral metabolism has been discussed. Its potent effect on cerebral function was demonstrated by experiments where it was given in a concentration of 30 per cent and evoked in the EEGs of all subjects high-voltage, rhythmic delta waves. It was shown also that the slow waves so produced were not inhibited (as is said to be the delta response to hyperpnoea) by a large increase in blood sugar. Whether this means a difference between these delta frequencies that is merely one of production or one of anatomical origin is not clear.

A further problem is posed by the somewhat complex relationship existing between alpha and delta frequencies and consciousness. Some explanation of this may be found in the work done on cats by Gellhorn (1953a). He concludes from his experiments that "high" carbon dioxide eliminates the reactivity of the hypothalamic-cortical system, while preserving the responsiveness of specific cortical projection areas, and he outlines the mechanism of the activating and inhibitory systems of hypothalamus and thalamus. If one applies this theory, it means that 30 per cent carbon dioxide blocks the hypothalamic-cortical system and produces narcosis while, at the same time, there is a release of the inhibitory system regulated by the intralaminar thalamic nuclei which leads to the appearance of delta frequencies in the EEG.

The fact that delta frequencies can be produced by both hyperpnoea and carbon dioxide inhalation suggests that both carbon dioxide lack and excess act by some such mechanism as outlined above. It has long been suspected that paroxysmal, bilaterally synchronous discharges originate in diencephalic structures having access to homologous areas of both hemispheres. Such an origin has been demonstrated for spike and wave rhythm and, in addition, the slow wave component has been obtained by stimulation of the intralaminar region of the thalamus (Jasper and Droogleever-Fortuyn 1946; Hunter and Jasper 1949; Jasper 1949). It does not seem far-fetched, therefore, to suggest that the delta waves produced by carbon dioxide lack and excess are diencephalic in origin.

The ultimate mechanisms involved and the chain of events that connects cortical changes with overbreathing or carbon dioxide inhalation remain in doubt. But there seems to be evidence for the presence of a homeostatic mechanism protecting the brain against untoward biochemical changes and indications that individual variation may depend on the relative stability of this device. There may be recalled in this connection the theories of Darrow (1946) regarding cortico-thalamo-hypothalamic relations; and the effect on cerebral regulation of autonomic factors in cerebral bloodflow. There must also be remembered the apparently direct effect of change in carbon dioxide tension in the neuronal atmosphere upon neurone excitability. It must be confessed, however, that the man-

ner in which all these factors link up remains obscure.

The fact that 30 per cent carbon dioxide is a useful therapeutic weapon raises a point of interest. Roth (1951) investigating the changes in the EEG produced by ECT, concluded that the primary effects of convulsive therapy are on diencephalic structures. He suggested further that the changes produced constitute a biologically purposive response of the homeostatic centres of the brain, tending to restore a stable pattern of cerebral function. There is a tempting correlation here with carbon dioxide inhalation therapy in regard to both site and mode of action.

The function of diencephalic centres in the genesis of delta rhythms in the EEG, in the response of patients to psychiatric treatments and in the whole question of homeostasis, is one demanding further investigation. It has been suggested that the thalamic reticular system has a regulating function and indeed it has been named by Earl Walker the "intracerebral division of the autonomic system". The autonomic side-effects of psychiatric treatments are everyday observations, but it is possible that they signify events of more importance than has been realised.

The work of Darrow already quoted suggests an important role for the autonomic nervous system in EEG patterns. Earlier work that may be mentioned is that of Hoagland *et al.* (1938) who found that slow activity in the EEG appeared simultaneously with pulse changes during affective stimulation. Moreover, recordings from the region of the hypothalamus showed changes before cortical recordings. From this one might surmise that the autonomic nervous system is implicated in the regulation of the EEG, since it has a direct interaction with affective states.

Comment has already been passed on the lack of a suitable test of autonomic function that is both adequate and simple to apply. In these studies, use was made firstly of the oculo-cardiac reflex and secondly of a test depending on the reactions of systolic blood pressure to autonomic drugs. The findings confirm that these tests are useful and can to some extent measure autonomic balance. This factor was shown to be important in the EEG response to overbreathing and its correlation with cerebral stability was demonstrated. One concluded that the individual variation in overbreathing response could be thus explained.

The relative stability of individuals in groups D, d and O can be viewed from the standpoint of cybernetics and this gives rise to interesting speculation. Ashby (1954) has pointed out that in the brain "if any part or subsystem should become less than normally stable it will exert more than the normal degree of influence on the brain's activities. Conversely, should any part become excessively stable, that part will be unable to cooperate adequately in the activity of the whole". This suggests that those subjects with a group d response are functioning in a better adjusted manner than those in the other groups. Group D subjects may be prone to disorders depending on instability of the higher autonomic centres; while group O subjects are maladjusted because of excessive stability. The suggestions of Gibbs and Kety and their co-workers that a delta response to hyperpnoea indicates a defective vasoconstrictor response, and the present findings regarding the autonomic lability of group D subjects, may have added importance in relation to this concept. For example, there may be recalled the role attributed to vasomotor lability in such disorders as migraine and cerebral haemorrhage (Meyer and McLardy 1950). On the face of it, it seems probable that group D subject would be more liable to such disorders.

It has been shown that the response to hyperpnoea in repeated EEGs in the same subject is almost constant. This means that it is a more or less permanent or constitutional characteristic and it now seems reasonable to infer that this individual quality equates with autonomic balance. Sympathetic or parasympathetic predominance in the individual, or lability in either direction, can affect the response of the cerebral vasomotor system and the EEG pattern. One believes that such an autonomic effect is visible, not only under the stress of overbreathing, but also in the resting

record. Has it not been found that the majority of subjects with slow wave responses on hyperpnoea have slow activity in their resting records ? It is not surprising, therefore, that attempts have been made to correlate basic personality structure with EEG patterns on the one hand (Lemere 1936; Saul *et al.* 1949), and with autonomic response on the other (Lacey *et al.* 1952). It has been pointed out by Kennard (1953) that, both in normals and in those with psychological disturbances, the EEG pattern seems to be related to personality type. Moreover, instability of personality and instability of EEG pattern seem to coincide in many instances. This is a neat and attractively straightforward hypothesis. It might be possible to verify it by such a technique as was used in section IV of these studies, where patients were examined by both hyperpnoea and autonomic stimulation. The range of patients was not wide enough to allow valid conclusions along these lines and a control group of normals was also lacking; but an interesting finding was the appearance of schizophrenics in the group highly responsive to both hyperpnoea and autonomic drugs. This raises the question of what is meant by instability of personality and how it can be measured.

Attempts have been made to measure a single element in the EEG, for example the alpha index, and thus show a statistical difference between normals and psychotics. Kennard expresses the conviction that any single element is far less significant than judgements based on each record as a whole; and, further, that the abnormalities which break into the pattern rather than the pattern itself constitute the significant difference. In this latter respect, I feel hyperpnoea occupies an important place in the EEG examination and the delta response may provide a useful index. It is likely that the sensitivity of the EEG in psychiatric disorders is due to, or is an aspect of, biochemical factors affecting cell respiration. For example, studies have suggested the presence of oxygen deficiency in certain types of schizophrenia, and a high percentage of schizophrenic and melancholic patients show a diminished excitability of the respiratory centres to carbon dioxide inhalations (McFarland 1952). Under the stress of overbreathing one might expect a relationship of this order to become more obvious. Evidence for this view has been provided by these studies.

An investigation of considerable interest in relation to such conclusions and speculations upon personality, psychiatric disorder and EEG pattern is that of Hodge *et al.* (1953). Of 100 delinquent boys they examined, 68 had EEG records showing low amplitude delta frequencies. Psycho-social assessments were made and certain of them (thought by the authors to have a common factor and named "ductility") were found to be significantly associated with the presence of such delta rhythms. Further EEG studies along these lines, it was felt, might confirm an association between electrical "abnormality" and delinquency as a social phenomenon and might cast light on the interdependence of brain physiology and psychological development.

As already implied, the problem of the aetiology and significance of slow waves in the EEG is merely part of the greater question regarding all frequencies. Delta rhythms are worthy of study because they often correlate with abnormal clinical conditions and signify abnormal cerebral functioning. Full understanding cannot be expected, however, until the whole range of frequencies and wave forms is fitted into the jig-saw of electrophysiology and it, in turn, takes its place in the pattern alongside biochemistry on the one hand and psychiatry on the other. As Bishop (1952) has pointed out, every chemical process in a nerve cell is presumably represented by an electrical change, and every electrical phenomenon presumably correlates with mental functioning. Between the oxidative metabolism of nerve cells and mental behaviour, the record of electrical activity is a natural bridge. However, much constructive effort is still required, not only from the biochemist, but also from the psychiatrist who hopes to understand brain function in terms of electrical activity.

SUMMARY

The factors influencing the response of the EEG to hyperpnoea have been investigated experimentally. To the six known factors, a seventh has been added — that of inherent "stability". Tests were devised to measure this "stability" in terms of autonomic balance. It was shown that the EEG response to hyperpnoea can be categorised as D, d and O, according to the amount of slow activity evoked; and that group D subjects are autonomically more labile than group O.

Carbon dioxide was shown to have a potent effect on the EEG and speculation was offered (among other things) regarding its site of action when used therapeutically.

Interrelations were suggested between basic personality structure, EEG patterns and autonomic balance.

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REFERENCES

ASCHNER, B. *Wien. klin. Wschr.*, **1908**, *21*: 1529.

ASHBY, W. R. The application of cybernetics to psychiatry. *J. ment. Sci.*, **1954**, *100*: 114-124.

ASMUSSEN, E. and BUCHTHAL, F. A method for the rapid determination of the degree of forced breathing. *EEG Clin. Neurophysiol.*, **1949**, *1*: 503-504.

BARNES, T. C. and AMOROSO, M. D. Physiological factors that determine the effects of hyperventilation on the EEG. *Anat. Rec.*, **1946**, *94*: 418.

BISHOP, G. H. *The Biology of Mental Health and Disease*. Cassell. **1952**, pp. 159-161.

BLINN, K. A. and NOELL, W. K. Continuous measurement of alveolar carbon dioxide tension during the hyperventilation test in routine electroencephalography. *EEG Clin. Neurophysiol.*, **1949**, *1*: 333.

BREMER, F. Considérations sur l'origine et la nature des "ondes" cérébrales. *EEG Clin. Neurophysiol.*, **1949**, *1*: 177-193.

COHN, R. *Clinical Electroencephalography*. McGraw-Hill, **1949**.

COHN, R. Occipital alpha rhythm; study of phase variations. *J. Neurophysiol.*, **1948**, *11*: 31-37.

DAGNINI, GUISEPPE. *Bull. d. Sci. med.*, **1908**, *79*: 380.

DAGNINI, GUIDO. *Cuore e circolaz.*, **1937**, *21*: 9.

DARROW, C. W. The EEG and psychophysiological regulation in the brain. *Amer. J. Psychiat.*, **1946**, *102*: 791-798.

DARROW, C. W. and GRAF, C. G. The relation of the EEG to photometrically observed vasomotor changes in the brain. *J. Neurophysiol.*, **1945**, *8*: 449-461.

DARROW, C. W., GREEN, J. R., DAVIS, E. W. and GAROL, H. W. Cholinergic influence on high potential slow waves of the EEG. *Fed. Proc.*, **1944**, *3*: 8.

DARROW, C. W., JOST, H., SOLOMAN, A. P. and MERGENER, J. C. Autonomic indications of excitatory and homeostatic effects on the EEG. *J. Psychol.*, **1942**, *14*: 115-130.

DAVIS, H. and WALLACE, W. Factors affecting changes produced in the EEG by standardized hyperventilation. *Arch. Neurol. Psychiat.*, Chicago, **1942**, *47*: 606-625.

DEMPSEY, E. W. and MORISON, R. S. The production of rhythmically recurrent cortical potentials after localised thalamic stimulation. *Amer. J. Physiol.*, **1942**, *135*: 293-300.

DROOGLEEVER-FORTUYN, J. D. and JASPER, H. H. Thalamic centres controlling rhythmic electrical activity of the cortex. *Proc. XVII Internat. Physiol. Congr.*, Oxford, **1947**, 368-369.

DUSSER DE BARENNE, J. G. and MCCULLOCH, W. S. The direct functional interrelation of sensory cortex and optic thalamus. *J. Neurophysiol.*, **1938**, *1*: 176-186. And; Sensorimotor cortex, nucleus caudatus and thalamus opticus. *Ibid.*, **1938**, *1*: 364-377.

ECCLES, J. C. An electrical hypothesis of synaptic and neuromuscular transmission. *Nature*, **1945**, *156*: 680-683.

ENGEL, G. L., FERRIS, E. B., STEVENS, C. D., LOGAN, M. and WEBB, J. P. The syndrome of hyperventilation. *J. Lab. clin. Med.*, **1946**, *31*: 474-476.

FUNKENSTEIN, D. H., GREENBLATT, M. and SOLOMON, H. C. Psychophysiological study of mentally ill patients. *Amer. J. Psychiat.*, **1949**, *106*: 16-28.

FUNKENSTEIN, D. H., GREENBLATT, M. and SOLOMON, H. C. An autonomic nervous system test of prognostic significance in relation to ECT. *Psychosom. Med.*, **1952**, *14*: 347-362.

GELLHORN, E. On the physiological actions of carbon dioxide on cortex and hypothalamus. *EEG Clin. Neurophysiol.*, **1953**a, *5*: 401-413.

GELLHORN, E. The physiological basis of the carbon dioxide therapy of psychoneuroses. *J. ment. Sci.*, **1953**b, *99*: 357-373.

GELLHORN, E. *Autonomic Regulations*. New York Intersc. Publ., **1943**, pp. 164-165.

GELLHORN, E. and YESINICK, L. Effect of oxygen lack and the inhalation of carbon dioxide on chemically induced convulsions. *Amer. J. Physiol.*, **1941**, *133*: 290.

GIBBS, F. A., WILLIAMS, D. and GIBBS, E. L. Modification of the cortical frequency spectrum by changes in carbon dioxide, blood sugar, and oxygen. *J. Neurophysiol.*, **1940**, *3*: 49-58.

GREENBLATT, M., FUNKENSTEIN, D., MILLER, D. and RINKEL, M. EEG patterns from the base of the brain. *Amer. J. Psychiat.*, **1947**, *103*: 749-757.

HEPPENSTALL, M. E. The relation between the effects of the blood sugar levels and hyperventilation on the EEG. *J. Neurol. Neurosurg. Psychiat.*, **1944**, *7*: 112-118.

HILL, D. and WATTERSON, D. EEG studies of psychopathic personalities. *J. Neurol. Psychiat.*, **1942**, *5*: 47-65.

HILL, L. and FLACK, M. The effect of excess of carbon dioxide and of want of oxygen upon the respiration and the circulation. *J. Physiol.*, **1908**, *37*: 77-111.

HOAGLAND, H. *Colloid Chemistry*, Alexander, J., New York, **1944**, pp. 762-785.

HOAGLAND, H., CAMERON, D. E., RUBIN, M. A. and TEGELBERG, J. Emotion in man as tested by the delta index of the EEG. *J. Gen. Psychol.*, **1938**, *19*: 227 and 247.

HOAGLAND, H. Discussion upon papers. Effects of anoxia on the EEG, by Finesinger, J. E. *et al.* and Brazier, M. A. B. *Arch. Neurol. Psychiat.*, Chicago, **1946**, *56*: 728-729.

HODGE, R. S., WALTER, V. J. and WALTER, W. G. Juvenile delinquency: an electrophysiological, psychological and social study. *Brit. J. Deling.*, **1953**, *3*: 1-18.

HUNTER, J. and JASPER, H. H. Effects of thalamic stimulation in unanaesthetised animals. *EEG Clin. Neurophysiol.*, **1949**, *1*: 305-324.

IGERSHEIMER, W. W. Cold pressor test in functional psychiatric syndromes. *Arch. Neurol. Psychiat.*, Chicago, **1953**, *70*: 794-801.

JASPER, H. H. Diffuse projection systems: the integrative action of the thalamic reticular system. *EEG Clin. Neurophysiol.*, **1949**, *1*: 405-420.

JASPER, H. and DROOGLEEVER-FORTUYN, J. Experimental studies on the functional anatomy of petit mal epilepsy. *Res. Publ. Ass. nerv. ment. Dis.*, **1946**, *26*: 272-298.

JEWESBURY, E. The EEG in doubtful cases of epilepsy. *Lancet*, **1952**, *1*: 1029-1031.

KENNARD, M. A. The EEG in psychological disorders. *Psychosom. Med.*, **1953**, *15*: 95-115.

KETY, S. S. and SCHMIDT, C. F. The effects of active and passive hyperventilation on cerebral blood flow, cerebral oxygen consumption, cardiac output, and blood pressure of normal young men. *J. Clin. Invest.*, **1946**, *25*: 107-119.

KETY, S. S. and SCHMIDT, C. F. The effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men. *J. Clin. Invest.*, **1948**, *27*: 484-492.

KING, E. J., HASLEWOOD, G. and DELORY, G. Microchemical methods of blood analysis. *Lancet*, **1937**, *1*: 886-892.

LACEY, J. I., BATEMAN, D. E. and LEHN, R. V. Autonomic response specificity and Rorschach colour responses. *Psychosom. Med.*, **1952**, *14*: 256.

LEAKE, C. D. and WATERS, R. M. Anaesthetic properties of carbon dioxide. *Anesth. Analges.*, **1929**, *8*: 17-19.

LEMERE, F. The significance of individual differences in Berger rhythm. *Brain*, **1936**, *59*: 366-375.

LENNOX, W. G. and COBB, S. Epilepsy from standpoint of physiology and treatment. *Medicine*, **1928**, *7*: 105-290.

LENNOX, W. G., GIBBS, F. A. and GIBBS, E. L. Relationship in man of cerebral activity to blood flow and blood constituents. *J. Neurol. Psychiat.*, **1938**, *1*: 211-225.

LIBERSON, W. T. and STRAUSS, H. EEG studies: Slow activity during hyperventilation in relation to age. *Proc. Soc. Exper. Biol. Med.*, **1941**, *48*: 674.

LLOYD-SMITH, D. L. The EEG during hyperventilation followed by apnoea. *EEG Clin. Neurophysiol.*, **1950**, *2*: 289-296.

LOEVENHART, A. S., LORENZ, W. F. and WATERS, R. M. Cerebral stimulation. *J. A. M. A.*, **1929**, *92*: 880-883.

MCCULLOCH, W. S. Modes of functional organization of cerebral cortex. *Fed. Proc.*, **1947**, *6*: 448-452.

MCFARLAND, R. A. *The Biology of Mental Health and Disease.* Cassell, **1952**, pp. 335-355.

MCQUARRIE, I. and ZIEGLER, M. R. Mechanism of insulin convulsions; effects of varying partial pressures of atmospheric oxygen, nitrogen and carbon dioxide. *Proc. Soc. Exper. Biol. Med.*, **1938**, *39*: 525-527.

MEADOW, A., GREENBLATT, M., FUNKENSTEIN, D. and SOLOMON, H. Relationship between capacity for abstraction in schizophrenia and physiologic response to autonomic drugs. *J. nerv. ment. Dis.*, **1953**, *118*: 332-338.

MEDUNA, L. J. *Carbon Dioxide Therapy.* Chas. Thomas, Springfield, Ill. **1950**.

MEYER, A. and MCLARDY, T. *Recent Progress in Psychiatry.* Churchill. **1950**, *2*: 284-323.

MILLS, J. N. Hyperpnoea induced by forced breathing. *J. Physiol.*, **1946**, *105*: 95-116.

POLLOCK, G. H. Quoted in Stein and Pollock (**1949**).

POLLOCK, G. H., STEIN, S. N. and GYARFAS, K. Central inhibitory effects of carbon dioxide: III Man. *Proc. Soc. Exper. Biol. Med.*, **1949**, *70*: 291.

ROTH, M. Changes in the EEG under barbiturate anaesthesia produced by electro-convulsive treatment and their significance for the theory of ECT action. *EEG Clin. Neurophysiol.*, **1951**, *3*: 261-280.

RUBIN, M. A . Effect of hyperventilation on the EEG of schizophrenic and nonpsychotic subjects. *Arch. Neurol. Psychiat.*, Chicago, **1942**, *48*: 968.

SAUL, L. J., DAVIS, H. and DAVIS, P. A. Psychological correlation with the EEG. *Psychosom. Med.*, **1949**, *11*: 361-376.

SCHMIDT, C. F. Present state of knowledge concerning the intrinsic control of the cerebral circulation and the effects of functional derangements in it. *Fed. Proc.*, **1944**, *3*: 131.

SCHWAB, R. S. In discussion of paper by Davis and Wallace (1942). *Arch. Neurol. Psychiat.*, Chicago, **1942**, *47*: 624-625.

SCHWOB, R. A. et MONNIER, M. Un cas de névrose végétative avec arrêt du cœur et automatisme ventriculaire pendant la compression oculaire. *Rev. Neurol.*, **1936**, *65*: 421-426.

STEIN, S. N. and POLLOCK, G. H. Central inhibitory effects of carbon dioxide: II Macacus rhesus. *Proc. Soc. Exper. Biol. Med.*, **1949**, *70*: 290.

THERON, P. A. Peripheral vasomotor reactions as indices of basic emotional tension and lability. *Psychosom. Med.*, **1948**, *10*: 335.

TINEL, J. *Le système nerveux végétatif.* Masson, Paris. **1937**.

WALTER, W. G. *Recent Progress in Psychiatry.* Churchill, **1950**, *2*: 76-93.

WALTER, W. G. The technique and application of electroencephalography. *J. Neurol. Psychiat.*, **1938**, *1*: 359-385.

WALTER, V. J. and WALTER, W. G. The central effects of rhythmic sensory stimulation. *EEG Clin. Neurophysiol.*, **1949**, *1*: 57-86.

WENGER, M. A. The measurement of individual differences in autonomic balance. *Psychosom. Med.*, **1941**, *3*: 427.

WENGER, M. A. Stability of the measurement of autonomic balance. *Psychosom. Med.*, **1942**, *4*: 94-95.

WENGER, M. A. and ELLINGTON, M. The measurement of autonomic balance in children: Method and normative data. *Psychosom. Med.*, **1943**, *5*: 241-253.

WENGER, M. A. and ELLINGTON, M. Preliminary study of the significance of measures of autonomic balance. *Psychosom. Med.*, **1947**, *9*: 301.

WILDER, J. *Wien. klin. Wschr.*, **1931**, *44*: 1299-1304.

WILLIAMS, D. The significance of an abnormal EEG. *J. Neurol. Psychiat.*, **1941**, *4*: 257-268.

WYKE, B. D. Brain function and blood sugar: Observations based on a case of islet cell adenoma of pancreas. *EEG Clin. Neurophysiol.*, **1952**, *4*: 339.

Reference: **MORRICE, J. K. W. Slow wave production in the EEG, with reference to hyperpnoea, carbon dioxide and autonomic balance. *EEG Clin. Neurophysiol.*, 1956, *8*: 49-72.**

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DÉCLENCHEMENT RÉFLEXE DE L'ACTIVITÉ CONVULSIVE

G. C. LAIRY [1]

Laboratoire de neuro-physiologie clinique et expérimentale,
Hôpital Henri-Rousselle, Paris

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L'objet de ce travail n'est pas l'épilepsie réflexe en général; il se limite à l'étude du rôle d'une afférence ou d'une série d'afférences dans la facilitation convulsive immédiate ou tardive, compte tenu de divers facteurs tels que topographie de la décharge, terrain, qualité des stimulations ...

Le problème clinique des décharges convulsives réflexes a été envisagé sous l'angle des phénomènes de répercussivité par André-Thomas (1929), de l'épilepsie réflexe par Critchley (1935) et Kinnier Wilson (1935), des phénomènes post-émotionnels par Ajuriaguerra (1948) ..., ces divers cadres cliniques se recoupant et s'intriquant assez étroitement. Il nous a paru que ce sujet méritait d'être actuellement reconsidéré au double point de vue de la neuro-physiologie et de l'électro-encéphalographie.

La physiologie classique, avec les données d'Amantea et de Clementi, celles très contestées de Danielopolu, n'aborde que le problème partiel de la facilitation post-afférentielle d'un foyer cortical convulsif et ne peut expliquer qu'une infime partie des cas cliniques. La neurophysiologie des dix dernières années a profondément remanié les conceptions classiques sur l'intégration centrale des afférences en ajoutant à la connaissance des systèmes de projection spécifiques, dévolus aux seuls instruments des fonctions de relation, celle des systèmes a-spécifiques réglant l'activité corticale dans sa totalité et dont dépendent, entre autres, les états de conscience et nombre d'états subjectifs. Une telle évolution, en matière d'épilepsie, permet de comprendre certaines inter-relations complexes que la clinique a longtemps pressenties, et que la physiologie classique laissait de côté, par exemple l'importance des facteurs affectivo-émotionnels dans le déclenchement des décharges convulsives.

La technique EEG se prête tout particulièrement à l'étude des décharges convulsives réflexes; elle en élargit considérablement le registre en permettant d'appréhender en plus des crises, toute une gamme de phénomènes infra-critiques; elle permet en outre d'en préciser le point de départ, la topographie, la diffusion (dont la crise clinique n'est souvent que la conséquence), enfin les relations avec les niveaux fonctionnels de base.

RÉSULTATS

Il faut distinguer d'une part les décharges réflexes immédiatement consécutives à une stimulation, d'autre part les effets plus tardifs ou plus prolongés que cette stimulation peut entraîner. Nous envisagerons successivement ces deux aspects du problème et les questions qu'ils soulèvent.

I. — DÉCHARGES CONVULSIVES RÉFLEXES IMMÉDIATES

Du point de vue EEG, ces décharges peuvent être localisées ou généralisées: leur modalité de déclenchement paraît cependant être semblable.

1. *Modalités de déclenchement.*

a) Lorsqu'une décharge convulsive réflexe se produit au niveau d'un foyer cortical lésionnel ou irritatif, le siège de ce foyer n'est pas nécessairement l'aire de projection du stimulus efficace. Son apparition est d'ordinaire liée à une mise en jeu de systèmes a-spécifiques, et peut survenir à la faveur de réactions d'activation, de sursaut, de désactivation ou sous l'effet de stimulations rythmiques:

i. Activation (fig. 1, 1); c'est-à-dire passage d'un état fonctionnel donné à un état

[1] Chargée de recherches à l'Institut National d'Hygiène.

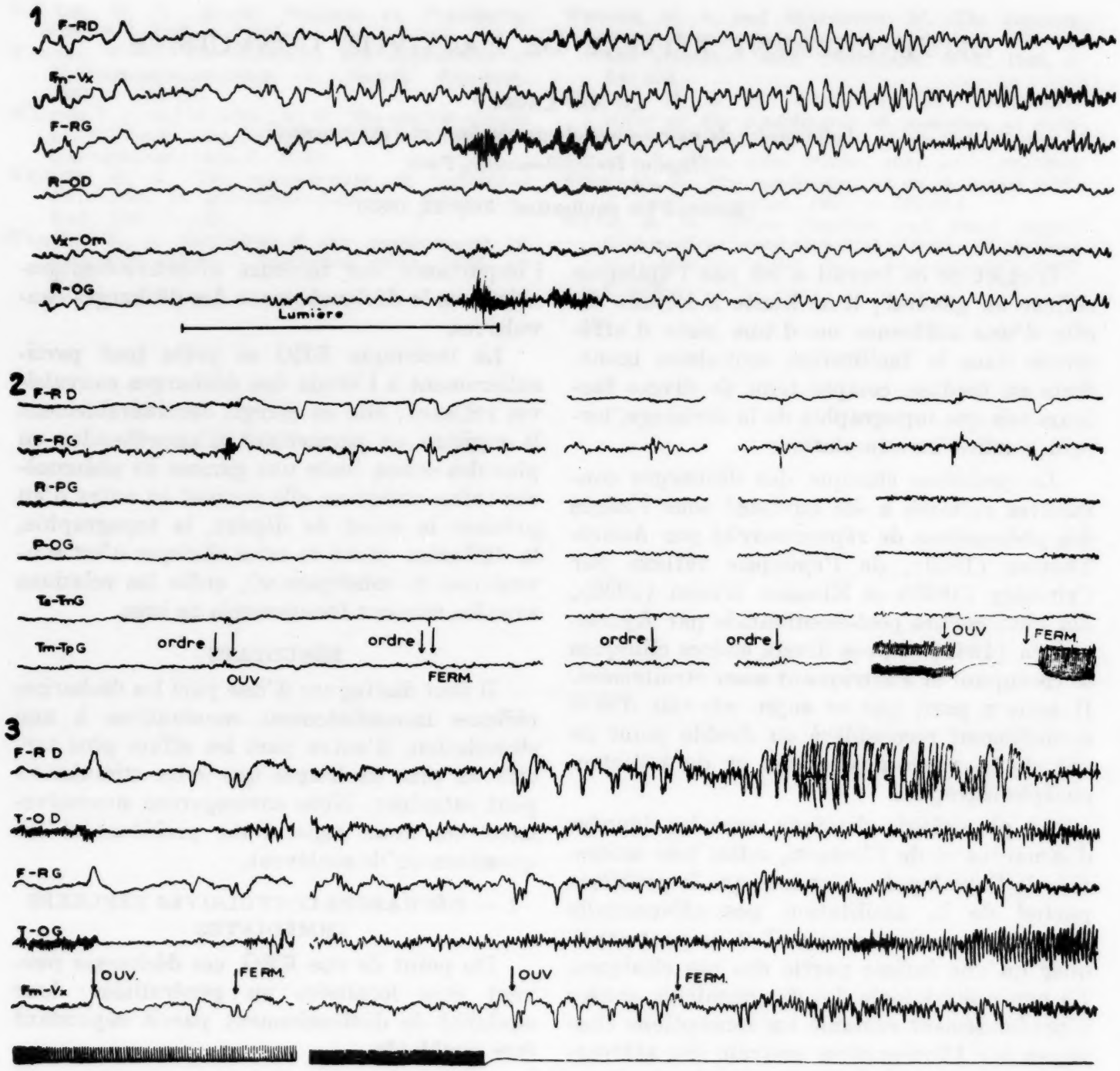


Fig. 1

Décharges convulsives post-afférentielles localisées

1. L. 35 ans. Empyème sous-dural frontal gauche paramédian — Sub-coma. Crises très fréquentes déclenchées par n'importe quelle stimulation.

EEG: tracé globalement ralenti. Foyer frontal gauche et frontal médian de pointes élargies sporadiques. Crise provoquée par l'illumination des yeux: renforcement du foyer suivi, au bout de 10 sec. d'une crise électrique et clinique.

2. M. 30 ans. Ablation d'un astrocytome frontal gauche 6 mois auparavant. Pose d'or radio actif sur la tranche de section. Aucun signe actuel d'hypertension intra-crânienne ni de récidive.

EEG: tracé subnormal. Pointes très aiguës frontales gauches, chaque fois qu'on donne un ordre au malade; pas de décharges de pointe pour les autres stimulations.

3. B. 27 ans. Crises vertigineuses et psycho-motrices. Pas de foyer EEG pré-critique; foyer temporal gauche post-critique.

EEG: crise provoquée par la S.L.I. La décharge de pointes temporales gauches apparaît au bout de deux minutes de stimulation, au moment où la réaction d'arrêt est abolie (d'après Lairy et Fischgold, *EEG Clin. Neurophysiol.*, **1953**).

d'activité plus grande; une réaction d'arrêt ou d'éveil est alors visible sur les autres dérivations suivant que le sujet est ou non vigile; ces cas se superposent aux données expérimentales de Lairy, Parma et Zanchetti (1951);

état de moindre activité, par exemple, retour au tracé alpha au décours d'une réaction d'arrêt ou passage de l'état vigile à l'endormissement;

iv. Stimulations rythmiques (fig. 1, 3); la stimulation lumineuse intermittente peut

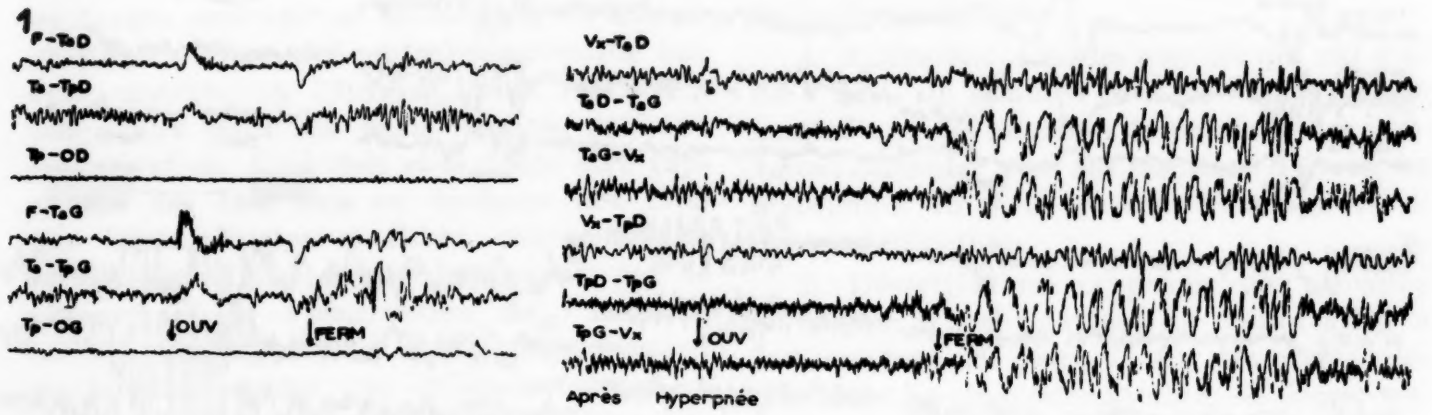


Fig. 2

Décharges temporales survenant à la faveur d'une désactivation.

1. H. 14 ans. Anoxie à la naissance. Depuis l'âge de 4 ans, crises généralisées et « absences temporales ».

EEG: rythme de fond un peu ralenti à 7 c/sec.; foyer de complexes pointe-ondes dégradés temporal gauche à la fermeture des yeux. Après hyperpnée, la fermeture des yeux provoque de longues décharges infra-cliniques.

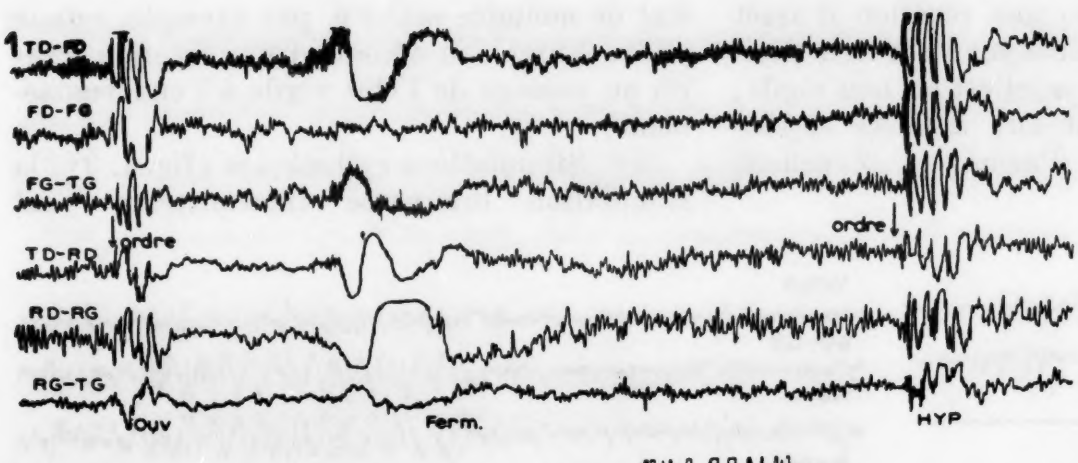
2. B. 58 ans. Traité pour paralysie générale 20 ans auparavant. Crises nocturnes psychomotrices avec confusion, agitation désordonnée, tentatives de défenestration.

EEG: tracé vigile normal; tendance à l'endormissement spontané, les phases de dépression de l'alpha s'accompagnant de pointes temporales droites disparaissent lors des réactions d'éveil; chez ce malade la crise spontanée est à type de dépression globale de l'activité alpha et du foyer.

ii. Réaction de sursaut ou tout au moins de surprise (fig. 1, 2); la décharge survient alors uniquement lors d'une stimulation inattendue, qu'il y ait ou non activation globale;

iii. Désactivation (fig. 2), c'est-à-dire passage d'un état fonctionnel donné à un

aboutir à la précipitation d'une décharge convulsive localisée; elle n'agit pas alors directement sur le foyer mais indirectement en modifiant le fond sur lequel ce foyer s'inscrit et en rendant ce fond favorable à l'expression du foyer.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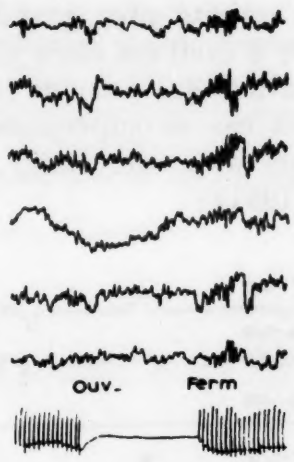
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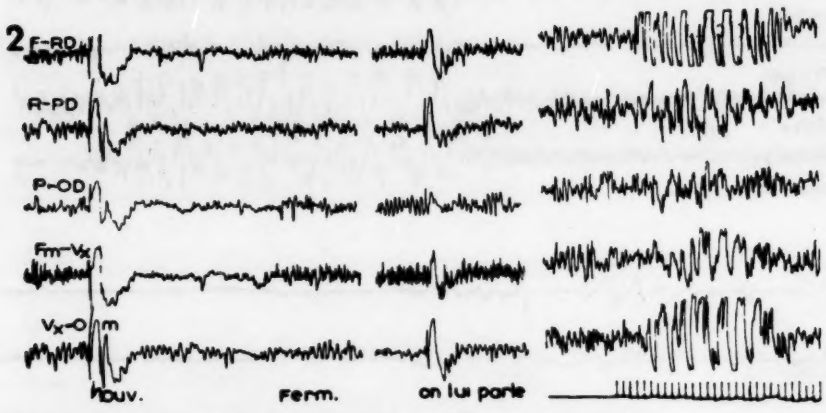
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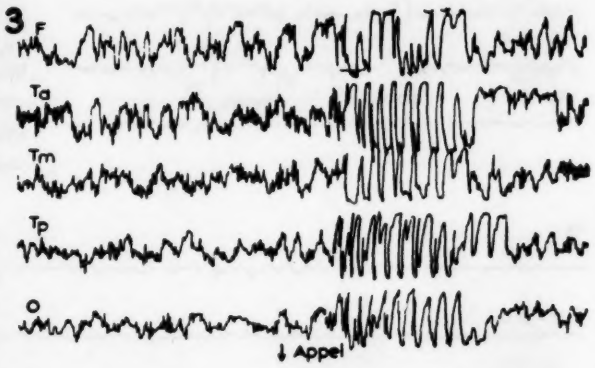
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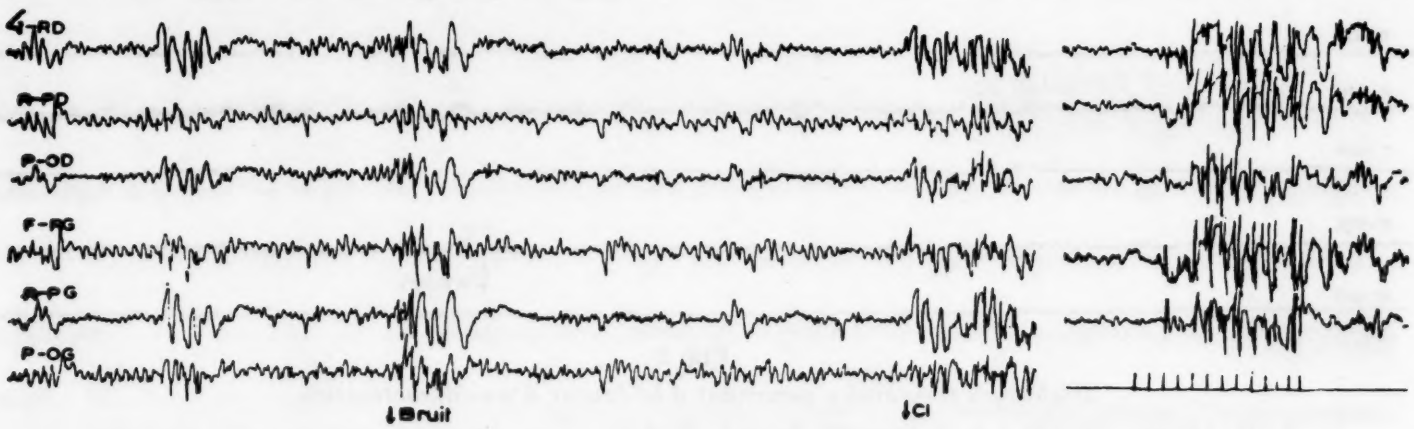
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Le déclenchement d'une activité convulsive locale, à la faveur d'une activation globale ou d'une réaction de sursaut, peut s'observer quel que soit le siège du foyer ainsi facilité. Rappelons ici les observations de Gibbs et Gibbs (1947), selon lesquelles le brusque réveil d'un malade qui présente des décharges convulsives infra-cliniques au niveau des régions pré-centrales, provoque une crise motrice. A l'inverse, seuls les foyers temporaux nous ont paru facilités par une désactivation. Ceci doit sans doute être rapproché des faits mis en évidence dès 1948 par Gibbs, Fuster et Gibbs, concernant la sensibilisation des foyers temporaux par le sommeil et de l'observation de Passouant (1951), que l'épilepsie de l'endormissement est le plus souvent une épilepsie temporale.

b) Les décharges convulsives réflexes diffuses sont, plus souvent que des crises généralisées, des bouffées de complexes pointe-ondes ou poly-pointe-ondes, et c'est dans l'épilepsie de type petit mal ou myoclonique que leur déclenchement post-afférentiel est le plus aisé. Sans doute, faut-il tenir compte du fait que ce sont des épilepsies à seuil d'excitabilité très bas. Mais aussi, faut-il penser que le point de départ de ces décharges, ou tout au moins, les systèmes impliqués dans leur production, sont voisins, sinon confondus, avec ceux qui sont mis en jeu par le type de stimulation efficace.

En effet, comme pour les décharges réflexes localisées leur apparition est souvent liée à un effet d'activation, ou de désactivation, une réaction de sursaut ou de surprise, ou à des stimulations rythmiques. D'une certaine électivité pour l'une ou l'autre de ces modalités de déclenchement, découle en partie la forme clinique :

i. Activation : tous les auteurs qui ont étudié l'EEG du sommeil chez les comitiaux ont montré que des bouffées de pointe-ondes pouvaient coïncider avec des réactions d'éveil ; les myoclonies du réveil en sont l'exemple clinique caractéristique.

ii. Désactivation : rappelons, par exemple, la fréquence des bouffées de pointe-ondes à la fermeture des yeux, la fin d'une réaction d'arrêt et les observations cliniques des pycnoleptiques montrant que ces enfants ont surtout des absences aux moments d'inattention.

iii. Startle : l'élément sursaut, surprise, émotion, est la qualité essentielle du stimulus qui provoque entre autres, les crises cataplectiques.

iv. Stimulations rythmiques : crises audiogéniques ou photogéniques.

Chacune de ces formes est d'ailleurs rarement pure et des décharges convulsives sont souvent provocables par plusieurs types de stimulations chez le même malade.

Fig. 3

1. P. 8 ans. Enfant d'intelligence normale. Crises cataplectiques à la surprise, 10 à 12 par jour.
EEG : rythme de fond normal ; bouffées de complexes pointe-ondes à l'ordre inattendu. Stimulation lumineuse intermittente négative.
2. G. 18 ans. Crises généralisées sans aura depuis la naissance. Une crise par mois environ ; myoclonies du réveil. Débilité légère.
EEG : tracé ample et pointu. Bouffées de complexes pointe-ondes au claquement sec, à l'ordre inattendu et à la stimulation lumineuse intermittente.
3. B. 22 mois. Crises nocturnes.
EEG : sommeil à la vériane. Bouffées de complexes pointe-ondes lorsque sa mère l'appelle. Pas de bouffée auparavant lorsque l'appel provenait d'une personne inconnue.
4. P. 21 ans. Petit mal myoclonique. Début à 9 ans après émotion violente (bombardement pendant l'exode). Rares crises généralisées. Clonies permanentes des membres et de la tête. Arrêt du développement mental, troubles endocriniens.
EEG : rythme de fond ralenti à 6, 7 c/sec., nombreuses bouffées de complexes pointe-ondes spontanées, facilement provoquées et renforcées par n'importe quelle stimulation et surtout la stimulation lumineuse intermittente.
5. G. 4 ans. Arriération profonde. Une crise convulsive de grand mal par semaine environ.
EEG : rythme de fond très plat et lent, sans fréquences normales. La moindre stimulation (claquement sec, piqûre ...) provoque de longs paroxysmes de complexes pointe-ondes très dégradés, diffus, s'accompagnant d'une hypotonie (l'enfant assis se ramasse sur lui-même, la tête s'affaise un peu sur la poitrine) et, à la fin du paroxysme, des mâchonnements. La S.L.I. régularise le tracé au lieu de le sensibiliser.

2. *Conditions favorisantes.*

La facilité avec laquelle la décharge localisée ou diffuse peut être déclenchée, dépend de plusieurs facteurs dont les principaux nous ont paru être le terrain et la qualité du stimulus.

a) Le « terrain » (ce terme étant pris au sens le plus large et englobant tout ce qui conditionne le tracé sur lequel le stimulus est appliqué, à la fois structure constitutionnelle, état fonctionnel et modification pathologiques).

Le « terrain » favorable aux décharges convulsives réflexes peut être homologué à la prédisposition des physiologistes italiens. Rappelons d'ailleurs qu'Amantea n'entendait pas ce terme au sens strict de prédisposition constitutionnelle; il avait observé que des animaux primitivement non prédisposés, pouvaient le devenir en cours d'expérience, à la suite de modifications neuro-humorales.

Chez l'homme, il est parfois possible de rendre expérimentalement un terrain donné favorable au déclenchement des décharges post-afférentielles en le modifiant par des procédés chimiques (Cardiazol), physiques (S.L. I.) ou métaboliques (hyperpnée). Ainsi on peut, en réponse à une stimulation inattendue, obtenir tous les intermédiaires entre la pointe physiologique au vertex et la bouffée myoclonique (Bancaud, Bloch, Paillard 1954).

La pathologie réalise toute une gamme de terrains favorables. Suivant le niveau d'excitabilité centrale ou le degré de déficit de l'inhibition corticale, on obtient plus ou moins facilement ces décharges réflexes. Le degré extrême est réalisé par l'épilepsie myoclonique, type Unverricht où chaque stimulation, même neutre pour l'observateur ne fait que précipiter une décharge toujours imminente (fig. 3, 4). Des états de détérioration globale facilitent des décharges dégradées mais plus prolongées du fait qu'aucun frein cortical ne s'oppose à leur expression (fig. 3, 5).

b) La « qualité du stimulus». Nous avons signalé des différences de modalités réactionnelles inter-individuelles, certains sujets exprimant un mode préférentiel de décharges réflexes. Ce sur quoi nous voulons insister ici, ce sont les variations intra-individuelles. Certaines d'entre elles, sont bien connues. Chez un même malade, les décharges convulsives à la stimulation lumineuse intermittente peuvent apparaître pour un rythme d'éclairement défini et non pour un autre. Les sujets qui présentent des décharges réflexes aux stimulations activatrices n'en présentent pas pour n'importe quelle stimulation activatrice. Par exemple, (fig. 3, 3) cette petite fille de 2 ans, enregistrées sous sommeil, reste indifférente lorsque nous l'appelons par son nom, mais présente une bouffée de pointe-ondes lorsque sa mère l'appelle par son nom; l'on retrouve ici la notion de qualité affective du stimulus dont on connaît bien l'importance dans le déterminisme des réactions d'éveil. La plupart des stimulations réflexogènes agissent par leur « mode d'éprouvé » plus que par leur caractère sensoriel pur; l'effet de surprise, si important pour tous les phénomènes de répercussivité, le caractère pénible ou douloureux d'un stimulus, la charge affective ou émotionnelle qu'il comporte, sont des éléments essentiels de leur efficacité; la clinique nous offre de nombreux exemples de stimuli efficaces lorsqu'ils sont imprévus, et indifférents lorsqu'ils sont attendus ou répétés; de stimuli péniblement ressentis dont la simple évocation mentale, même en rêve, suffit à provoquer la crise; de stimuli qui n'agissent que lorsqu'ils ont provoqué un état affectif particulier comme par exemple dans l'épilepsie musicogénique. La figure 4 illustre l'importance de certaines stimulations à composante affective (réprimande, compliments) qui se révèlent plus efficaces que le startle dans le déclenchement de paroxysmes diffus infra-cliniques.

II. — DÉCHARGES RÉFLEXES PROLONGÉES OU TARDIVES

Les données précédentes ont trait aux décharges convulsives critiques ou infra-critiques immédiatement induites par une stimulation, ce caractère immédiat rendant d'ailleurs évidente leur relation avec le stimulus. Plus difficile à appréhender, et par là même plus discutables, sont les modifications post-afférentielles prolongées ou tardives dont la relation avec le stimulus reste sujette à caution. En clinique, ce problème est essentiellement celui des crises post-émotionnelles tardives;

les cliniciens sont d'ordinaire très sévères pour appeler réflexes les crises succédant à une émotion, et ne tiennent compte que de celles qui suivent de très près un choc émotionnel. « Mais », dit André-Thomas . . . « bien qu'une émotion ait précédé la crise d'assez loin, de quelques heures ou même davantage, on ne peut s'appuyer sur ce long délai pour lui refuser toute influence pathogénique. C'est qu'en effet, l'émotion est le point de départ

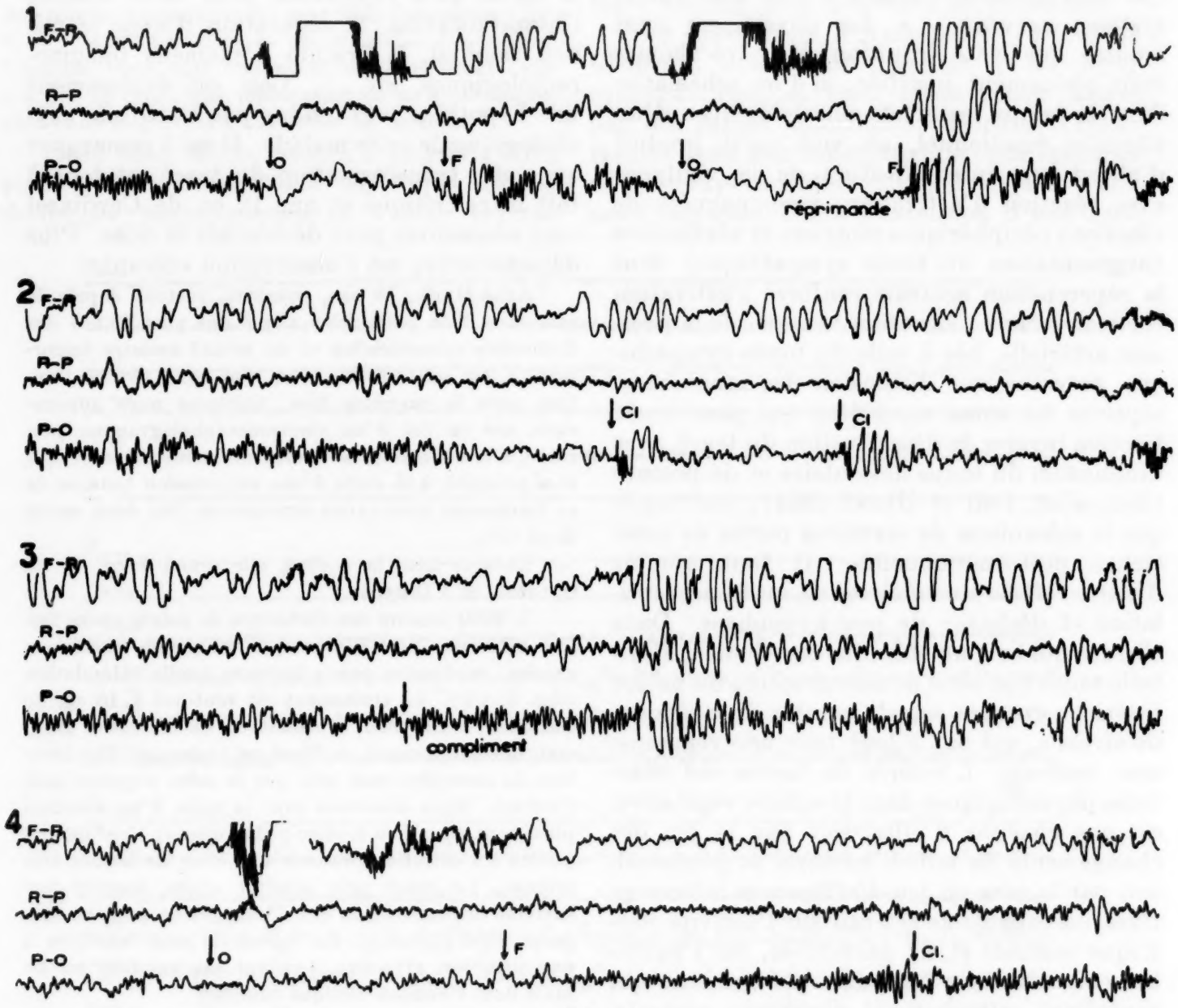

Fig. 4

F. 8 ans. Convulsions dans l'enfance.
Depuis 3 mois, 3 à 4 crises par jour avec cyanose, air hébété, quelques mouvements des doigts, pas de chute, parfois miction et sommeil post-critique.
Troubles caractériels: colères immotivées, difficultés scolaires, instabilité.

EEG: ondes lentes frontales droites permanentes; brèves bouffées de complexes pointe-ondes bilatérales, souvent réflexes.

1) la fermeture simple des yeux provoque une petite bouffée; la deuxième fermeture des yeux (avec réprimande à cause de l'instabilité permanente) provoque une bouffée beaucoup plus marquée.
2) brèves bouffées au claquement sec.
3) lorsqu'au contraire de 1. on félicite l'enfant pour une phase de tranquillité, on observe un renforcement de l'alpha pendant quelques secondes, suivi, à sa terminaison, d'une bouffée de complexes pointe-ondes. La S.L.I. sensibilise le tracé.
4) après 15 jours de traitement, disparition des paroxysmes réflexes.

d'un bouleversement qui se prolonge et passe par des états divers; il est difficile de savoir à quel moment, il exercera la répercussion la plus forte sur l'organisme; et puis le choc émotif entraîne des perturbations humorales qui sont en mesure d'agir à leur tour sur le système nerveux... » La physiologie nous montre que cette intuition d'André-Thomas était pleinement justifiée; si l'on schématise dans le temps les effets physiologiques d'un stimulus émotionnel, on voit qu'il produit d'abord une intensification de la vigilance avec réaction d'activation, accompagnées de réactions périphériques motrices et végétatives (augmentation du tonus sympathique) dont la répercussion centrale renforce l'activation corticale. Mais l'élévation brusque de la pression artérielle, liée à celle du tonus sympathique, entraîne une distension des zones baroceptives du sinus carotidien qui peut avoir l'action inverse de désactivation du tracé, avec diminution du tonus musculaire et de posture (Bonvallet, Dell et Hierel 1954); ceci explique le mécanisme de certaines pertes de conscience post-émotionnelles. Il faut ajouter d'autres effets secondaires tels qu'hyperventilation et décharge de post-hypophyse. Dans l'heure qui suit un stimulus émotionnel, s'installe toute une série de changements du milieu intérieur groupés sous le vocable de « réponse de stress », qui ont à leur tour une répercussion centrale. L'intérêt de toutes ces réactions physiologiques dans la sphère végétative, est que chacune d'elles, soit par le jeu des changements du milieu humoral et hormonal, soit par la mise en jeu d'afférences intéroceptives, est capable de retentir sur l'activité électrique centrale et, en particulier, sur l'équilibre existant entre les différents systèmes qui contrôlent cette activité électrique centrale. On voit qu'un stimulus émotionnel, s'il n'agit pas instantanément, peut créer toute une série de déséquilibres, échelonnés dans le temps dont nous avons vu que chacun d'eux peut être le plus favorable à telle ou telle forme d'activité convulsive.

Chez les malades épileptiques, il n'est pas possible de savoir, à moins d'une étude psycho-pathologique poussée, quelle est la stimulation ou la situation la plus intensément chargée de potentiel émotionnel. Certains cas privilégiés, nous ont permis de saisir sur des tracés successifs le reflet de ces traumatismes psychologiques. Ainsi, dans le cas illustré par la figure 5, la modification du tracé de fond, (fig. 5, 1 et 2) nous a paru en relation avec le stress qu'a représenté pour cette malade l'hospitalisation, la séparation d'avec le milieu familial, la crainte d'examens pneumo-radiologiques, etc.... Ceci est évidemment une hypothèse sous-tendue par l'attitude psychologique de cette malade. Il est à remarquer que cette transformation du tracé est tout à fait infra-critique et que 12 cc. de Cardiazol sont nécessaires pour déclencher la crise. Plus démonstrative est l'observation suivante:

Anne-Marie, 10 ans, présente, surtout depuis la naissance d'un petit frère (de 6 ans plus jeune) des difficultés caractérielles et un retard scolaire important. C'est en Octobre 1954, que nous voyons l'enfant pour la première fois. Quelques mois auparavant, sur la foi d'un électroencéphalogramme perturbé, elle a été soumise à un traitement anticonvulsif et a présenté, à la suite d'une suppression brusque de ce traitement deux crises convulsives (les deux seules de sa vie).

Lorsque nous la voyons, elle prend 7 cg. ½ de Gardénal et 1 Dihydan.

L'EEG montre des décharges de pointe-ondes isolées diffuses, infra-cliniques, à maximum postérieur gauche, renforcées par n'importe quelle stimulation (fig. 6, 1-2). Le traitement est renforcé à 10 cg. de Gardénal, 1 Dihydan, 1 bromiase. En décembre 1954, malgré ce traitement, le tracé est inchangé. Les troubles du caractère sont tels, que la mère supporte mal l'enfant. Nous discutons avec la mère d'un éventuel placement en milieu médico-pédagogique; l'enfant qui assiste à l'entretien présente une crise de larmes très intense. Le tracé pris aussitôt après, montre une extrême intensification des décharges de pointes, toujours infra-cliniques. En raison de cette réaction à une situation affective, l'enfant est montrée au Dr Male dont l'examen clinique conclue:

« Troubles du caractère à forme d'opposition, excitabilité, taquinerie, domination de la mère émotive et faible. Adaptation scolaire médiocre; dysorthographie, senestralité de base. Niveau mental normal, mais ralentissement dû au traitement. »

A partir de cette date, le traitement est progressivement supprimé. De plusieurs entretiens psychothérapiques avec la mère et l'enfant, résulte une nette amélioration du comportement de l'enfant dans le milieu familial (la famille n'envisage plus le placement), et une amélioration de la scolarité: l'enfant reste dans une classe d'enfants plus jeunes, mais passe de la place de 23ème à celle de 7ème en trois mois.

Le tracé pris le 30 Avril 1955, montre la presque complète disparition des décharges diffuses. On relève seulement la présence de pointes très sporadiques temporales antérieures droites (fig. 6, 5). En cours de tracé, nous reparlons à l'enfant d'une hospitalisation possible; on assiste alors à une facilitation des pointes temporales qui sont plus fréquentes (fig. 6, 6); cet effet ne dure qu'une vingtaine de secondes. L'enfant reste sans traitement médicamenteux; elle n'a pas de crise; une rééducation de sa dysorthographie et de sa gaucherie contrariée est en cours.

Cette observation montre à la fois l'effet possible d'un traumatisme psychique sur les décharges paroxystiques et l'effet inverse d'une amélioration des décharges parallèlement à celle du comportement.

DISCUSSION

1° La facilitation post-afférentielle d'un foyer localisé pose une série de problèmes.

Des expériences d'Amantea et surtout de Clementi, il semblait découler qu'un foyer convulsif cortical était électivement activé par des influx spécifiques. Moruzzi (1946) résume ainsi leur conception de cette épilepsie réflexe expérimentale... « Epilepsie purement corticale, liée à l'extension d'une acti-

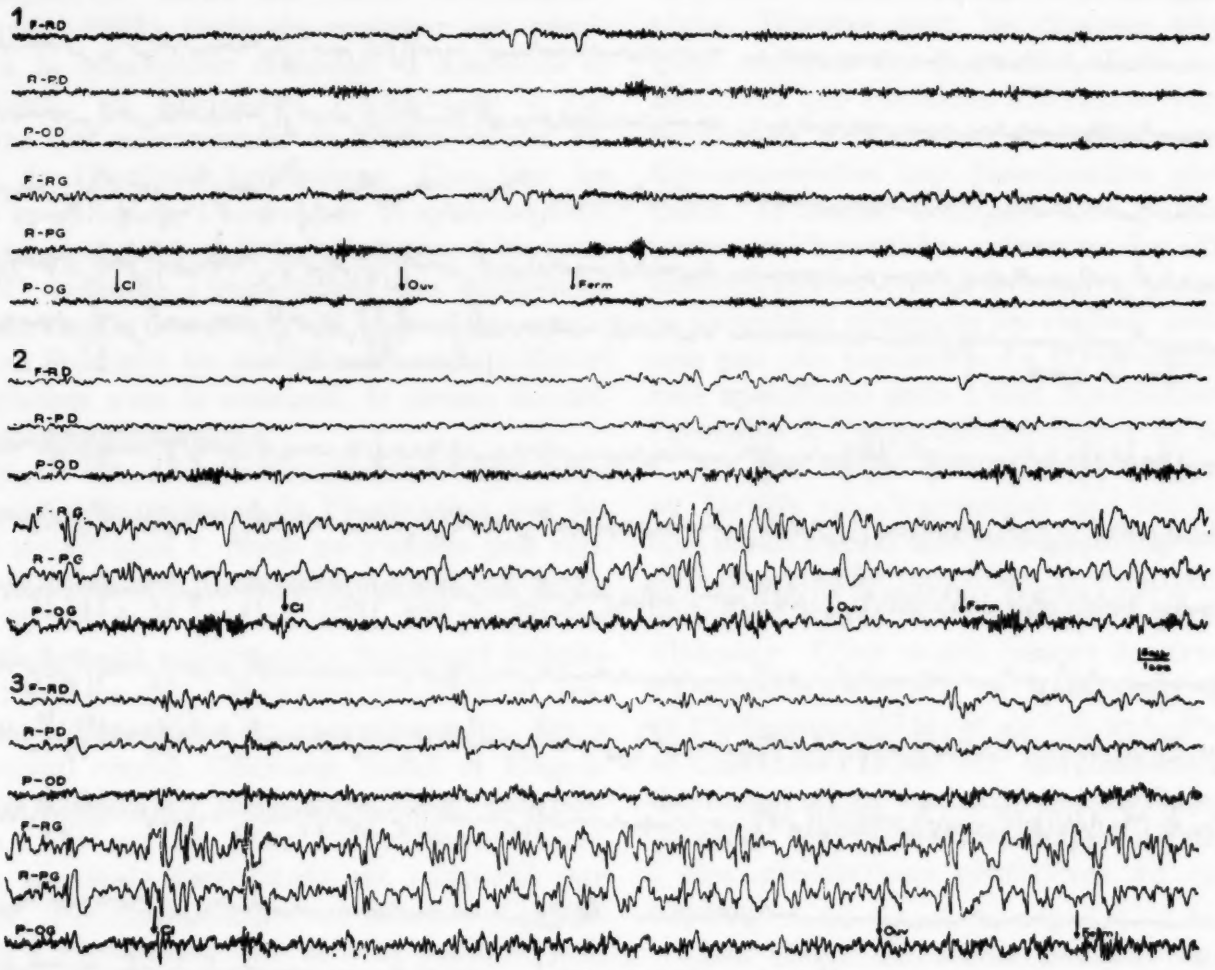

Fig. 5

B. 20 ans. Débile légère. Crises de l'aire supplémentaire motrice gauche.

1) malade examinée en consultation, entourée de ses parents.

EEG: tracé sub-normal; quelques ondes lentes frontales gauches.

2) (4 jours après 1) La malade est hospitalisée depuis la veille. Supporte affectivement mal la séparation d'avec la famille.
Pas de nouvelle crise; pas de modification du traitement.

EEG: complexes pointe-ondes dégradés sub-continus sur la région antérieure gauche paramédiane. Le claquement sec et l'ouverture des yeux bloquent les anomalies.

3) (suite de 2) après 7 cc. de Cardiazol, le claquement sec provoque une décharge paroxystique de pointe-ondes. L'ouverture des yeux renforce également les altérations. La crise survient pour 12 cc. de Cardiazol.

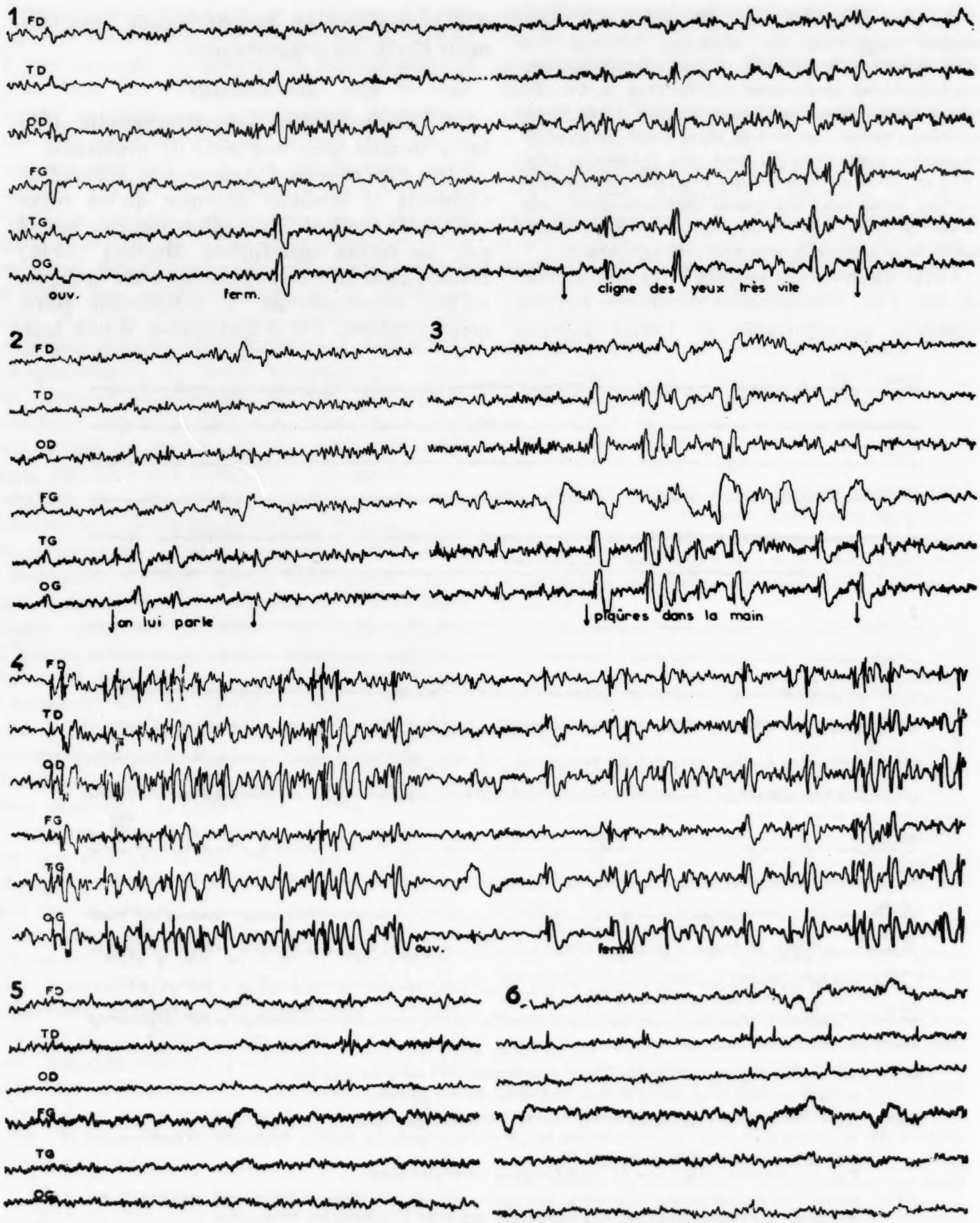

Fig. 6

A. 10 ans. cf. observation clinique dans le texte.

EEG: 1. 2. 3. Répercussivité des complexes pointe-ondes pour toute une série de stimulations.
4. Aggravation du tracé après un traumatisme affectif (menace d'hospitalisation).
5. Après quelques mois de psychothérapie et de suppression thérapeutique, normalisation du tracé; persistance de pointes sporadiques temporales droites.
6. Renforcement des pointes lorsqu'on reparle à l'enfant d'une hospitalisation.

vité corticale locale par bombardement d'influx afférents spécifiques chez des animaux prédisposés. » Les résultats expérimentaux obtenus en 1951 (Arduini et Lairy, Lairy, Parma et Zanchetti) sont en contradiction avec ce point de vue et montrent que la facilitation — critique ou infra-critique — d'un foyer strychnique cortical peut être obtenue pour n'importe quelle stimulation et qu'elle est liée non pas à l'effet spécifique mais à l'action globale d'activation. La stimulation du système réticulaire de Moruzzi et Magoun produit le même effet que le stimulus sensitivo-sensoriel. Dans un travail d'ensemble, Moruzzi (1952) tente de concilier ces résultats à la conception classique d'Amantea et Clementi, en proposant l'hypothèse d'une dualité des mécanismes de précipitation réflexe de l'activité épileptique, l'un par les voies spécifiques, l'autre par le système réticulaire ascendant. A la même époque, Magoun (1952) souligne l'importance des influences sous-corticales sur l'activité convulsive corticale en étudiant les modifications de celles-ci en relation avec le sommeil, le stress, les stimulations rythmiques.

Quelle est, d'après l'expérience EEG chez l'homme, l'importance de l'activation par les voies spécifiques ? Nous ne l'avons pas rencontrée dans nos observations : ceci est peut-être dû au fait que les aires de projection spécifiques ont une étendue tellement réduite chez l'homme que l'épilepsie sensitive ou sensorielle élémentaires est exceptionnelle. Dans un travail récent, Chavany, Lobel et Hagenmuller (1955) en rapportent deux cas possibles. Un cas de crise réflexe avec lésion de la pariétale ascendante est rapporté par Foster, Penfield, Jasper et Madow (1949). Il est à remarquer que si leur malade présente des crises B. J. spontanées, les crises réflexes électivement provoquées par un choc sur le coude contro-latéral, sont des crises cataplectiques avec résolution tonique globale, ce qui illustre bien les interactions cortico-sous-corticales.

Boudouresques et Gastaut (1954) ont publié des crises réflexes à l'ingestion d'aliments dans 4 cas d'épilepsie temporale. Ces auteurs, rappelant que la projection corticale du vague se fait au niveau des aires dont l'atteinte peut donner l'épilepsie temporale, concluent « Il est vraisemblable que les afférences corticipètes vagales provoquées par dilatation ou tension gastrique sont responsables de la crise temporale en augmentant le tonus cortical de cette région et en permettant la décharge neuronique paroxystique caractéristique de l'épilepsie. »

En réalité, il faut souligner que la crise temporale réalise le plus souvent non pas l'embrasement paroxystique d'un foyer mais une dépression ou un ralentissement généralisés de toute l'activité électrique, que l'on peut interpréter comme une désactivation globale critique. D'autre part, les données physiologiques récentes de Bonvallet, Dell et Hiebel montrent que certaines afférences vagales déterminent, à l'inverse des afférences sensitivo-sensorielles une désactivation globale du tracé. Il semble donc que l'on puisse plutôt proposer l'hypothèse suivante : des afférences désactivatrices (dont il reste à prouver que la distension gastrique les réalise) produisent, non pas une excitation du foyer temporal par voie spécifique mais l'état fonctionnel global favorable à l'expression critique de ce foyer.

2° Les effets post-afférentiels prolongés ou tardifs ne s'expriment pas toujours par une modification morphologique du tracé ; au-delà de son effet immédiat, la stimulation peut changer l'aptitude réactionnelle à un stimulus ultérieur. C'est ce qui ressort des travaux de Pampiglione (1952), de Passouant, Cadilhac et Philippot (1951), et de Schwab, Passouant et Cadilhac (1954) sur les phénomènes d'adaptation ou au contraire de conditionnement possibles des réponses normales ou convulsives à des stimulations répétitives au cours du sommeil.

Les effets du stress peuvent également aboutir à une simple modification de l'aptitude réactionnelle à un stimulus ultérieur, c'est-à-dire une modification du « terrain ». Lairy, Parma et Zanchetti, étudiant la réactivité de foyers strychniques corticaux chez le lapin, montrent que le blocage est la réaction habituelle de l'animal placé dans des conditions le plus proche possible des conditions physiologiques à des stimuli non douloureux. La facilitation, par contre, survient, soit pour des stimuli douloureux, soit pour des stimuli

neutres appliqués dans des conditions non physiologiques, réalisant une situation de stress. A partir du moment, où les réactions de facilitation sont obtenues, elles survivent aux conditions qui ont déterminé leur apparition et il n'est plus possible, même en remettant l'animal dans les conditions antérieures, d'obtenir à nouveau les réactions de blocage pendant un temps plus ou moins long.

3° Qu'il s'agisse d'un changement de l'aptitude réactionnelle ou d'une modification de la morphologie du tracé, on voit l'importance du stress dans les phénomènes de facilitation. Ceci permet de comprendre nombre d'observations cliniques de Barker (1948), de Bartemeïer (1943), qui établissent des relations entre la fréquence des crises de leurs malades et certaines conditions psychologiques, en particulier, pour Berlin et Yeager (1952) l'état émotionnel des malades et de leur entourage familial.

Tous ces auteurs proposent, lorsque c'est possible, l'institution d'une psychothérapie des épileptiques comme adjuvant des thérapeutiques chimiques. Les études statistiques de Stanley Cobb (1940) montrent l'importance des résultats que l'on peut en attendre. Les données physiologiques et EEG que nous avons rapportées, tendent à justifier une telle attitude.

RÉSUMÉ ET CONCLUSION

La facilitation réflexe d'une activité convulsive localisée ou diffuse survient d'ordinaire à la faveur d'une rupture d'équilibre des systèmes a-spécifiques. Une afférence (ou une série d'afférences) peut provoquer une facilitation immédiate, liée à des réactions d'activation, de désactivation, de startle ou aux effets de stimulations rythmiques; elle peut avoir des effets secondaires en modifiant le terrain et l'aptitude réactionnelle à un stimulus ultérieur; enfin, elle peut être à l'origine d'une facilitation prolongée ou tardive. A côté de l'importance du terrain sur lequel le stimulus est appliqué et qui est à son tour influencé par ce stimulus, est soulignée l'importance de la qualité du stimulus; tant pour les effets immédiats que tardifs, la qualité affective ou émotionnelle du stimulus joue un rôle essentiel.

L'EEG, envisagé, non comme une méthode de diagnostic, mais comme une méthode d'investigation psychopathologique, permet l'étude des différents facteurs qui sous-tendent le déclenchement de l'activité convulsive. Il objective l'importance des facteurs psychologiques et peut aider à adapter à chaque malade une thérapeutique individuelle.

BIBLIOGRAPHIE

AJURIAGUERRA, J. DE. Emotions et troubles toniques paroxystiques. *L'Evol. Psychiat.*, **1948**, *9*: 1-35.

ANDRÉ-THOMAS. *Les phénomènes de répercussivité.* In Vol.2., Masson, **1929**.

ARDUINI, A. et LAIRY-BOUNES, G. C. Action de la stimulation électrique de la formation réticulaire du bulbe et des stimulations sensorielles sur les ondes strychniques corticales chez le chat « encéphale isolé ». *EEG Clin. Neurophysiol.*, **1952**, *4*: 503-512.

BANCAUD, J., BLOCH, V. et PAILLARD, J. Contribution EEG à l'étude des potentiels évoqués chez l'homme au niveau du vertex. *Rev. Neurol.*, **1953**, *89*: 399-418.

BARKER, W. Studies on epilepsy: the petit mal attack as a response within the central nervous system to distress in organism-environmental integration. *Psychosom. Med.*, **1948**, *10*: 73-94.

BARTEMEIER, L. H. Concerning the psychogenesis of convulsive disorders. *Psychoanal. Quart.*, **1943**, *12*: 330-337.

BERLIN, J. N. and YEAGER, C. L. Early investigation of the relationship between the EEGs and the emotional state in a few epileptic children. *EEG Clin. Neurophysiol.*, **1952**, *4*: 368.

BONVALLET, M., DELL, P., HIEBEL, G. Tonus sympathique et activité électrique corticale. *EEG Clin. Neurophysiol.*, **1954**, *6*: 119-144.

BOUDOURESQUES, J. et GASTAUT, H. Le « mécanisme réflexe » de certaines épilepsies temporales. *Rev. Neurol.*, **1954**, *90*: 157-158.

CHAVANY, J. A., LOBEL, G. et HAGENMULLER, D. Considérations sur l'épilepsie réflexe. *La Presse Médicale*, **1955**, *63*: 230-233.

COBB, ST. Psychiatric approach to the treatment of epilepsy. *Ann. J. Psychiat.*, **1940**, *96*: 1009-1022.

CRITCHLEY, M. Ueber Reflexepilepsie. *Schweiz. Arch. Psych. Neurol.*, **1935**, *35*: 256.

FOSTER, M., PENFIELD, W., JASPER, H. and MADOW, L. Focal epilepsy, sensory precipitation and evoqued eortical potentiels. *EEG Clin. Neurophysiol.*, **1949**, *1*: 349-356.

GIBBS, E. L., FUSTER, B. and GIBBS, F. A. Peculiar low temporal localization of sleep induced seizure discharge of psychomotor type. *Arch. Neurol. Psychiat.*, Chicago, **1948**, *60*: 95-96.

GIBBS, E. L. and GIBBS, F. A. Diagnostic and localizing value of EEG studies in sleep. *Res. Publ. Ass. nerv. ment. Dis.*, **1947**, *26*: 366-376.

LAIRY-BOUNES, G. C., PARMA, M. et ZANCHETTI, A. Modifications pendant la réaction d'arrêt de Berger de l'activité convulsive produite par l'application locale de strychnine sur le cortex cérébral du lapin. *EEG Clin. Neurophysiol.*, **1952**, *4*: 495-502.

MAGOUN, H. W. Recent contributions to seizure activation. *Epilepsia*, **1952**, *3*: 69-82.

MORUZZI, G. The physiologic mechanisms of the epileptic discharge. *Acta Psychiat. Neurol. scand.*, **1952**, *27*: 317-328.

MORUZZI, G. *L'épilepsie expérimentale.* Herman et Cie, éditeurs, **1950**.

PAMPIGLIONE, G. The phenomenon of adaptation in human EEG (a study of k complexes). *Rev. Neurol.*, **1952**, *87*: 197-198.

PASSOUANT, P., LATOUR, H. et CADILHAC, J. L'épilepsie morphéique. *Ann. méd.-psychol.*, **1951**, *109*: 526-540.

PASSOUANT, P., CADILHAC, J. et PHILIPPOT, M. Rythmicité du petit mal au cours du sommeil, décharges rythmiques généralisées et localisées. *Rev. Neurol.*, **1951**, *84*: 659-663.

PASSOUANT, P., SCHWAB, R. S., BRAZIER, M. A. and CASBY, J. Activation of the EEG during sleep with regular repetitive sounds every 2 to 10 seconds. *EEG Clin. Neurophysiol.*, **1952**, *4*: 382.

SCHWAB, R. S., PASSOUANT, P. et CADILHAC, J. Action des stimulations auditives rythmées sur le sommeil humain. *Montpellier Méd.*, **1954**, *45*: 501-514.

WILSON KINNIER, S. A. The Epilepsies. *Handbuch der Neurologie.*, **1935**, *17*: 1-87.

Reference: LAIRY, G. C. Déclenchement réflexe de l'activité convulsive. *EEG Clin. Neurophysiol.*, **1956**, *8*: 73-85.

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Special Courses in nine different neurological subjects will be presented by a selected faculty at the April 1956 meeting of the American Academy of Neurology in St. Louis, Missouri, on April 23, 24 and 25, 1956. Three courses will be given daily: Neuropathology, Infectious Diseases in Neurology, Clinical Electroencephalography and Electromyography, Convulsive Disorders, Neurologic Disorders in Infancy and Childhood, Neurochemistry, Injuries to the Nervous System, Current Advances in Neurology. Neurophysiology will require two days. In addition, the Academy will also present a Course for General Practitioners.

For details, write to Mrs. J. C. McKinley, Executive Secretary, 3501 East 54th Street, Minneapolis 17, Minnesota.

CHANGES IN THE ELECTROENCEPHALOGRAM ASSOCIATED WITH HYPOPITUITARISM DUE TO POST-PARTUM NECROSIS

ROBERT R. HUGHES, M.D. and V. K. SUMMERS, M.D.
Royal Southern Hospital and Walton Hospital, Liverpool, England

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The syndrome resulting from loss of the anterior pituitary has attracted much attention recently. While Simmonds first called attention to this in 1914, his clinical description has been much modified of recent years; Sheehan (1939) gave the first clear account of the clinical syndrome arising from post-partum necrosis of the gland, and Sheehan and Summers (1949) reviewed the clinical, biochemical and other features arising from destruction of the gland as a result of various types of pathology.

While certain aspects of this syndrome have been studied in great detail, the cerebral changes resulting from destruction of the gland have received relatively little attention. These patients show a considerable degree of mental torpor, they lack initiative, show little interest in home and friends, and settle into a state of placid inertia. Psychotic changes may occur and may consist of depression or melancholia; this high incidence of psychosis in post mortem reports may be due to the detailed inspection of the cranial contents made at autopsy on patients dying in mental hospitals and may not reflect the correct incidence of psychosis in pituitary necrosis. Many cases of this syndrome die in coma — sometimes hypoglycaemic in origin, sometimes due to sodium and chloride lack and sometimes to hypothermia.

In many cases coming to autopsy the brain has been reported normal. Sheehan and Summers (1949) reported that on careful examination of the hypothalamus histological changes have been apparent in a certain proportion of cases. "Among ten severe cases in which the hypothalamus was examined in detail, there were no lesions in three, a reduced number of cells in the supra-optic nuclei in one, some perivascular cuffing in the supra-optic region in two, gliosis in the tuberal region in two, and minor cellular changes in two cases." These authors also reported similar changes in some of the patients with only slight pituitary damage. They felt uncertain how far these changes were terminal in nature.

It would thus seem that so far as at present can be ascertained, changes in the brain associated with post-partum pituitary necrosis are inconstant; when present they consist of minor changes in the supraoptic area and these changes may well be terminal in origin.

The EEG in hypopituitarism.

There are few references in the literature to the EEG in post-partum hypopituitarism. The earliest reference is by Means, Herts and Lerman (1940) who mention a woman of 30 years (Case 3) with amenorrhoea, loss of libido and "myxoedema" following seven years after a post-partum haemorrhage. The authors state that "... even the electroencephalogram (slow alpha rhythm) was characteristic of myxoedema".

Hoffman, Lewis and Thorm (1942) in a paper reporting theta activity in 18 of 25 patients with Addison's disease state "it may be stated that we have encountered similar pictures very rarely in adult patients in the Phipps Clinic Laboratory, and pronounced only in a patient with Simmonds' disease."

Piaggio-Blanco *et al.* (1950) described two cases of "pituitary myxoedema", the second case is almost certainly post-partum necrosis of the pituitary gland and an unusually slow rhythm was noted (6 to 6½ c/sec.).

Thorn *et al.* (1951) noted the case of a woman of 34 years (Case PBBH 5A755), with hypopituitarism following a post-partum haemorrhage ten years previously; the electroencephalogram showed a slow rhythm which became normal on treatment with cortisone and thyroid.

Clarke, Franklin and Sahs (1951) report a case of post-partum pituitary necrosis where the electroencephalogram revealed a dominant rhythm of 7½ to 8½ c/sec.

Guinet, Favre-Gilly and Girard (1952) give details of a further case of post-partum necrosis where the basic rhythm had a frequency of 7-8 c/sec., but in addition there were some 5-6 c/sec. waves particularly on the right side.

Guinet *et al.* (1953) describe a patient of 41 years who had had a post-partum haemorrhage 3 years previously producing classical features of hypopituitarism. The electroencephalogram had a basic rhythm of 6-7 c/sec., there were no frequencies above 8 c/sec.

The reported cases of post-partum hypopituitarism in which an electroencephalogram has been taken are thus few in number but in general they suggest that the basic rhythm is slower than in the normal adult.

During the past few years we have been able to record the electroencephalogram in a number of cases of hypopituitarism; in 13 cases the syndrome had followed severe post-partum haemorrhage, and in one case (case 5) the syndrome started immediately after a pregnancy. We report these only. The only demonstrable lesion was hypopituitarism. In these cases due to post-partum pituitary necrosis there was no evidence of organic brain damage due to any other cause and the EEG changes may therefore reasonably be attributed to the pituitary necrosis.

Case histories.

As this paper is concerned primarily with the EEG changes in post-partum hypopituitarism it is unnecessary to give a full clinical history in each instance. The cases fulfil the criteria laid down by Sheeham (1939) and in almost every instance the diagnosis has been confirmed by him. In these cases there was a severe haemorrhage associated with childbirth, lactation did not occur, the pregnancy was followed by complete amenorrhoea, lethargy, anaemia, atrophy of the sexual organs, loss of libido and loss of the pubic and axillary hair. The results of certain biochemical investigations, etc. are given for each patient.

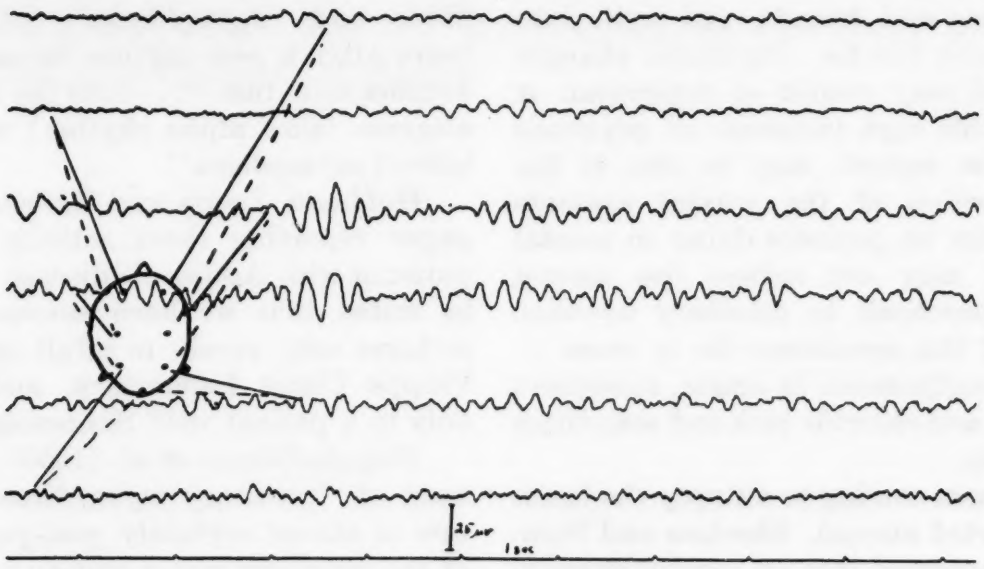

Fig. 1

Case H. 1.

T. D.

Post-partum haemorrhage in 1929 when 31 years old.

Clinically a severe case.

Dec. 1947.

Investigations —

Glucose tolerance test — flat curve, highest level 71 mg. per cent.

Serum Sodium — 285 mg. per cent.

Serum Potassium — 26 mg. per cent.

FTM — Complete achlorhydria.

13.12.50.

EEG — Constant generalised 5 c/sec. theta activity with an amplitude up to 30 μV.

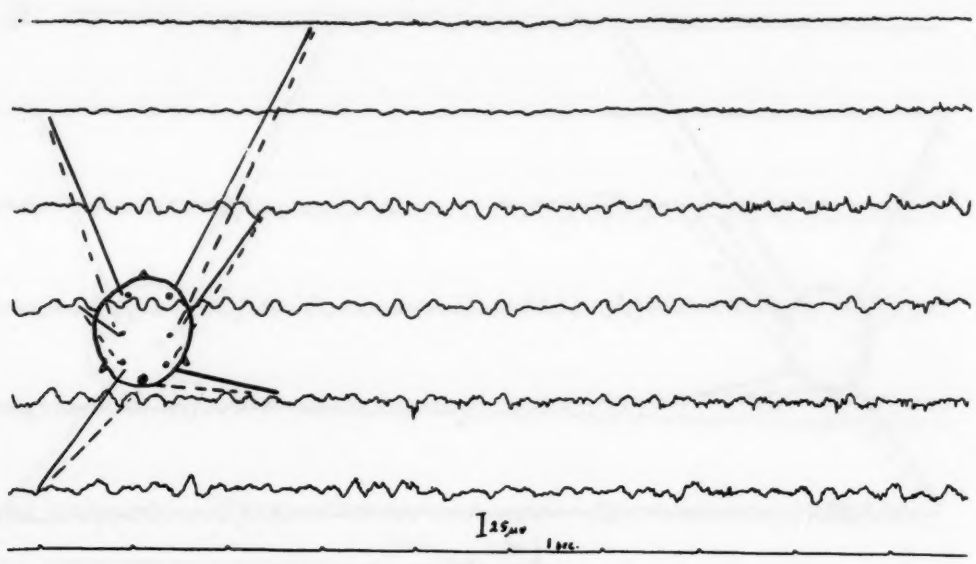

Fig. 2

Case H. 2.

C. G.

Post-partum haemorrhage in 1927 when 33 years old.

Clinically — a severe case, admitted in coma.

Treatment (prior to admission) Testosterone 100 mg. i-m weekly for the past 2 years.

9.1.52.

17 Ketosteroids 1.0mg./day.

10.1.52.

17 Ketosteroids 0.3 mg./day.

Corticosteroids nil/day.

EEG — Constant generalised 4 c/sec. theta activity with an amplitude up to 40 μV.

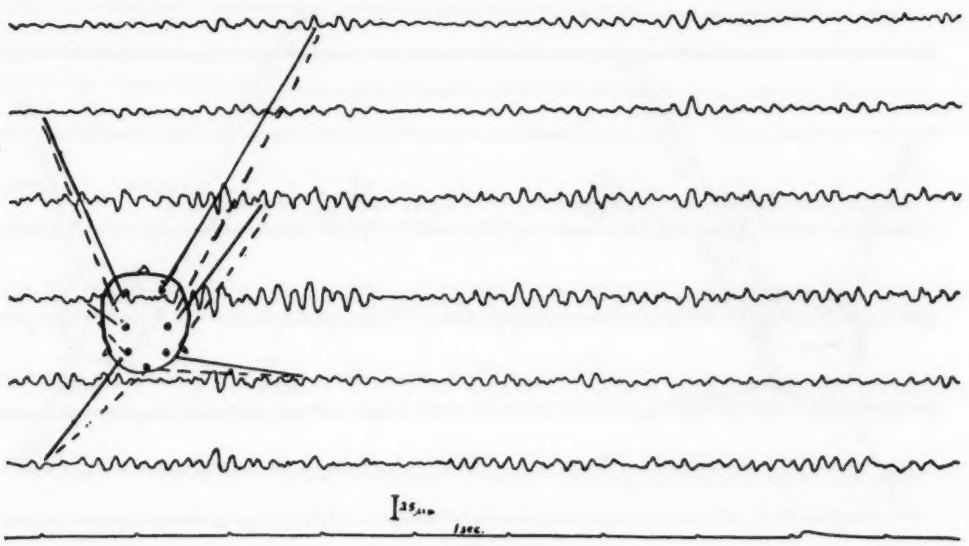

Fig. 3

Case H. 3.

E. B.

Post-partum haemorrhage in 1929 when 30 years.

Clinically — a severe case.

12.11.51.

Basal Metabolic Rate: minus 20 per cent.

EEG — Constant generalised 5-6 c/sec. theta activity with an amplitude up to 30 μV.

14.11.51.

17 Ketosteroids 0.1 mg./day.

EEG — Constant generalised 6 c/sec. theta activity with an amplitude up to 60 μV.

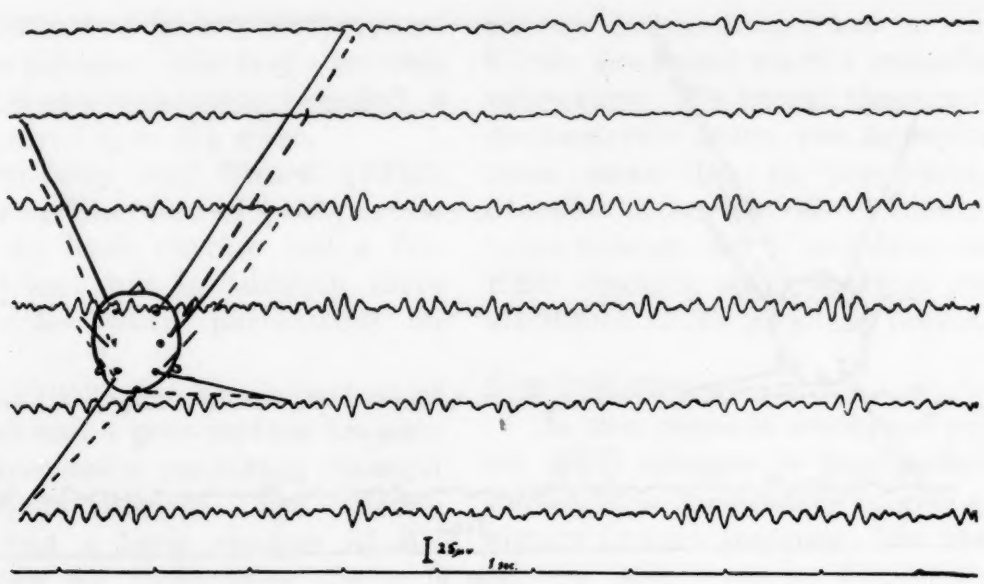

Fig. 4

Case H. 4.

A. A.

Post-partum haemorrhage in 1933 when 31 *years old.*

Clinically — a severe case.

7.12.50.

EEG — Generalised 5-6 c/sec. theta activity with an amplitude up to 30 μV.

5.1.51.

17 Ketosteroids — 0.25 mg./day.

9.1.51.

Basal Metabolic Rate: minus 30 per cent.

17.1.51.

EEG — Generalised 5-6 c/sec. theta activity with an amplitude up to 30 μV.

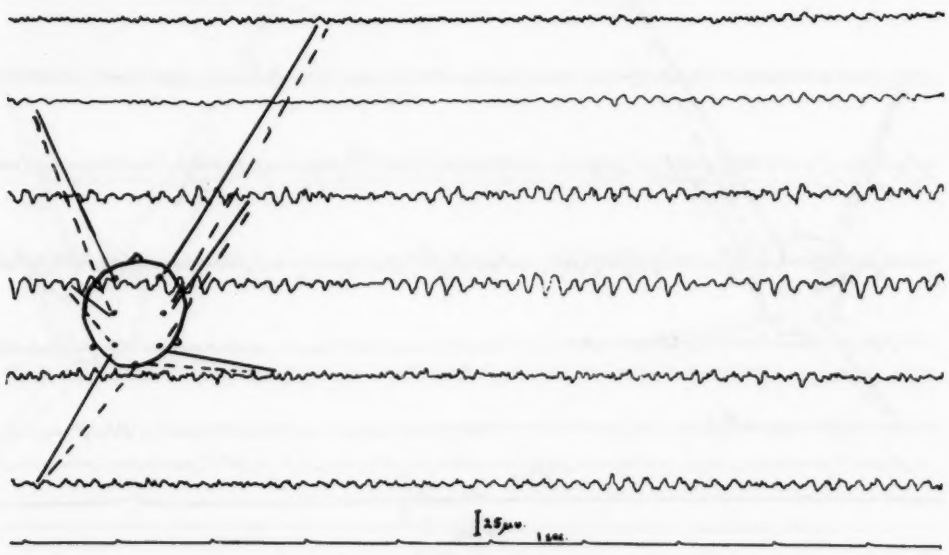

Fig. 5

Case H. 5.

M. R.

Condition started after last pregnancy in 1926 when 25 yrs.

No post-partum haemorrhage.

Clinically — a severe case.

17 Ketosteroids — 1.0 mg./day.

Basal Metabolic Rate — minus 30 per cent.

24.10.51.

EEG — Generalised 5 c/sec. theta activity with an amplitude up to 30 μV.

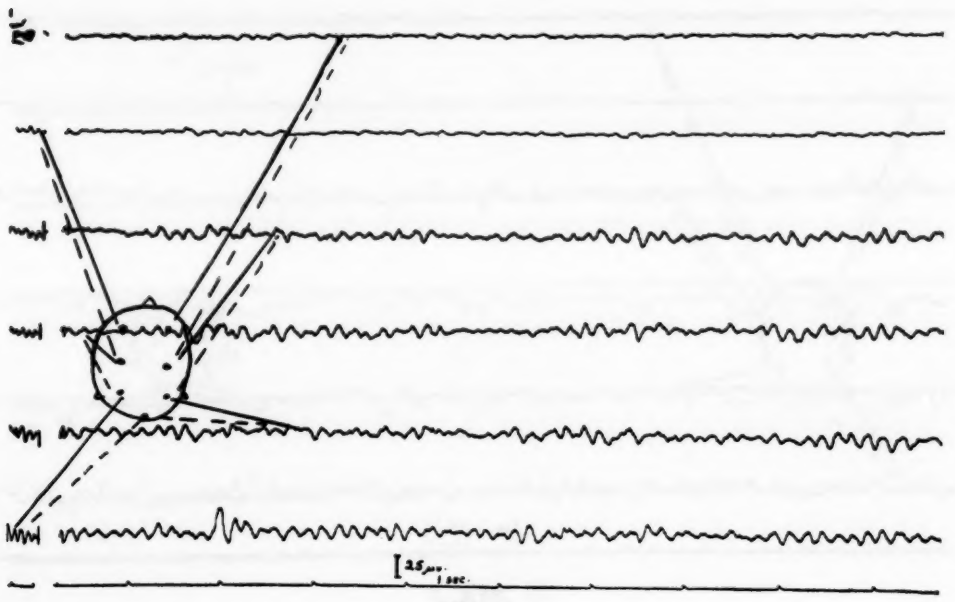

Fig. 6

Case H. 6.

M. M.

Post-partum haemorrhage in 1934 when 26 years old.

Clinically — a severe case.

20.11.50.

17 Ketosteroids — 0.12 mg./day.

25.11.50.

Basal Metabolic Rate: minus 21 per cent.

27.11.50.

EEG — Generalised 6.5 c/sec. theta activity with an amplitude up to 30 μV.

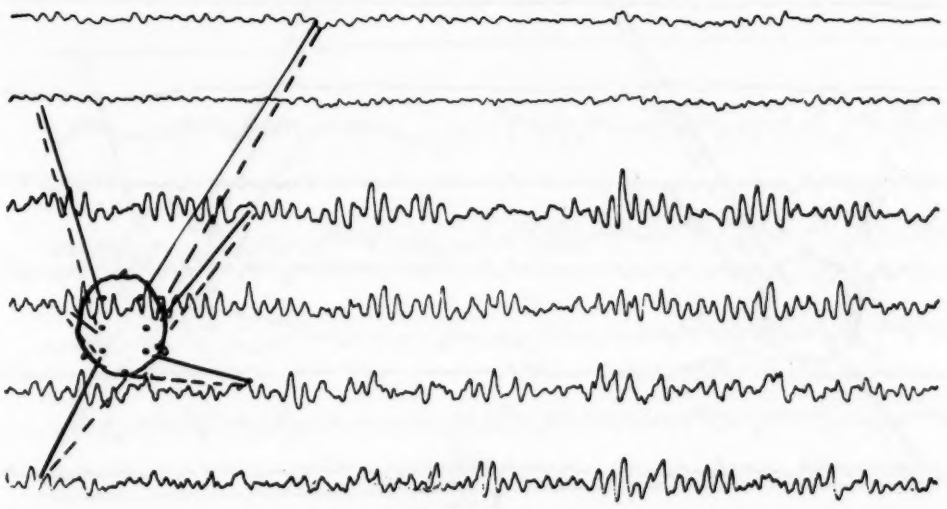

Fig. 7

Case H. 7.

E. H.

Post-partum haemorrhage in 1925 at 32 years old.

Clinically — a severe case.

19.1.51.

17 Ketosteroids — 0.25 mg./day.

Kepler Test — positive.

13.3.51.

17 Ketosteroids 0.12 mg./day.

15.3.51.

EEG — Generalised 6.5 c/sec. theta activity with an amplitude up to 50 μV.

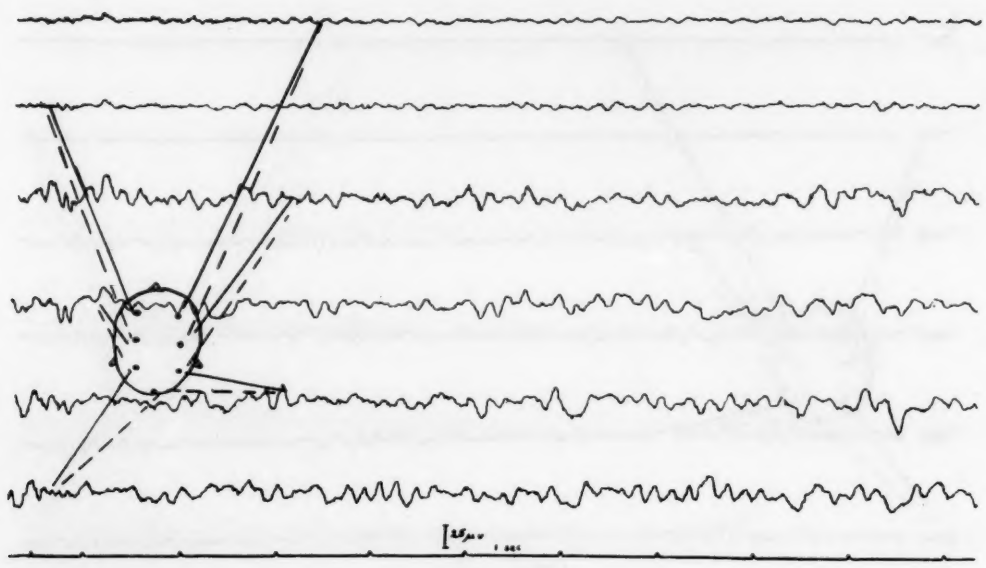

Fig. 8

Case H. 8.

E. P.

Haemorrhage after Caesarian Section in 1943 when 33 years old.

Clinically — a severe case.

Basal Metabolic Rate: minus 34 per cent.

17 Ketosteroids — 0.09 to 1.0 mg./day.

17.3.49.

Kepler Test — positive.

17.1.51.

EEG — Generalised 5-6 c/sec. theta activity with an amplitude up to 40 μV. A little 3 c/sec. delta activity present.

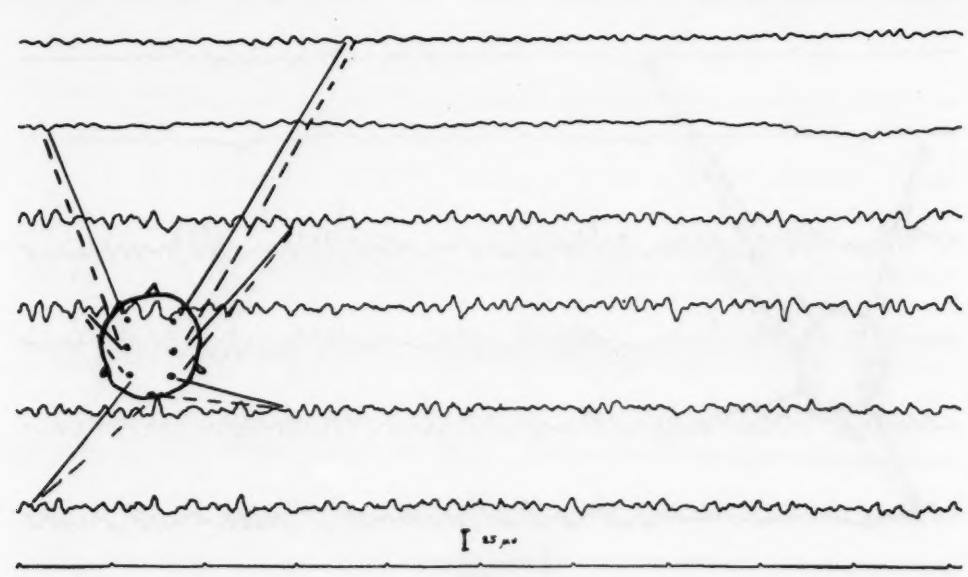

Fig. 9

Case H. 9.

E. E.

Post-partum haemorrhage in 1923 at 28 *years.*

Clinically — a severe case.

17.8.52.

17 Ketosteroids — 1.2 mg./day.

25.8.52.

17 Ketosteroids — 0.6 mg./day.

28.8.52.

Basal Metabolic Rate. minus 33 per cent.

23.9.52.

EEG — Generalised 5-6 c/sec. theta activity with an amplitude up to 40 μV.

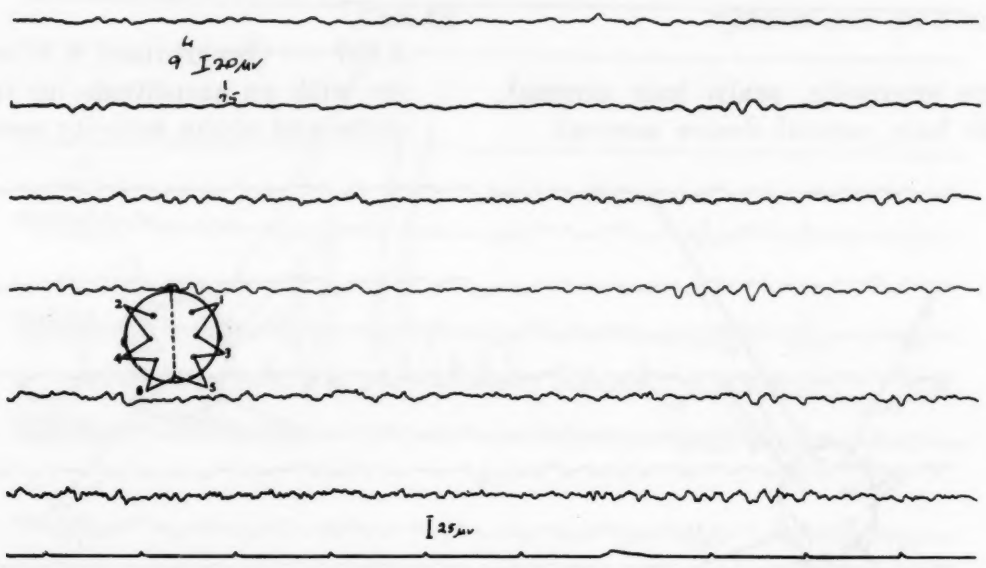

Fig. 10

Case H. 10.

M. H.

Post-partum haemorrhage in 1937 when 30 years old.

Clinically — a severe case.

1.12.52.

Kepler Test — markedly positive.

12.12.52.

17 Ketosteroids — 0.1 mg./day.

18.12.52.

EEG — Generalised 5-6 c/sec. theta activity with an amplitude up to 40 μV.

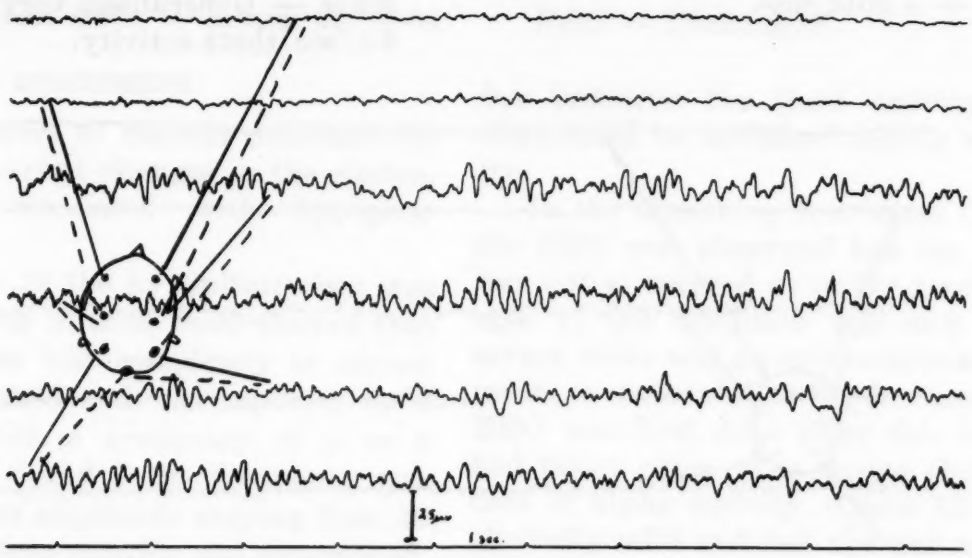

Fig. 11

Case H. 11.

C. B.

Post-partum haemorrhage in 1932 when 33 years old.

Clinically — a moderately severe case.

1943

Basal Metabolic Rate — minus 37 per cent.

17 Ketosteroids — 1.5 mg./day.

24.7.50.

Methyl Testosterone 20 mg. daily (under tongue).

Thyroid gr. ½ daily.

DOCA 5 mg. i-m weekly.

28.8.50.

DOCA discontinued.

Continue testosterone and thyroid.

Anahaemin 5 cc. i.m. weekly.

12.2.51.

Much more energetic, scalp hair normal, some pubic hair, sexual desire normal.

21.2.51.

EEG — Generalised 6 c/sec. theta activity with an amplitude up to 25 μV. Some delta and alpha activity seen.

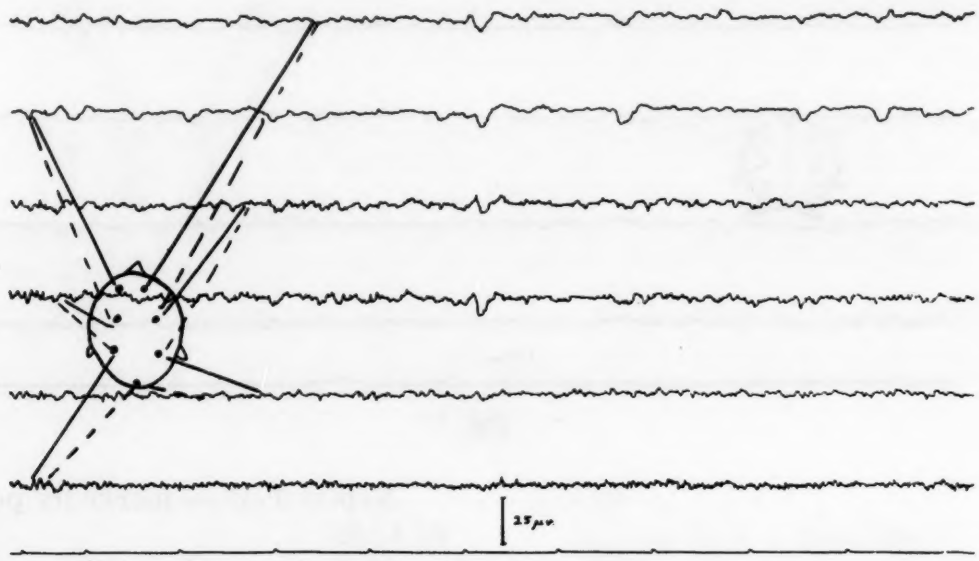

Fig. 12

Case H. 12.

E. H.

Post-partum haemorrhage in 1949 when 28 years old.

Clinically — a mild case.

Oct. '51.

Basal Metabolic Rate — minus 2 per cent.

Kepler Test — negative.

17 Ketosteroids 0.99 mg./day.

8.11.51.

EEG — Generalised very low amplitude 6 c/sec. theta activity.

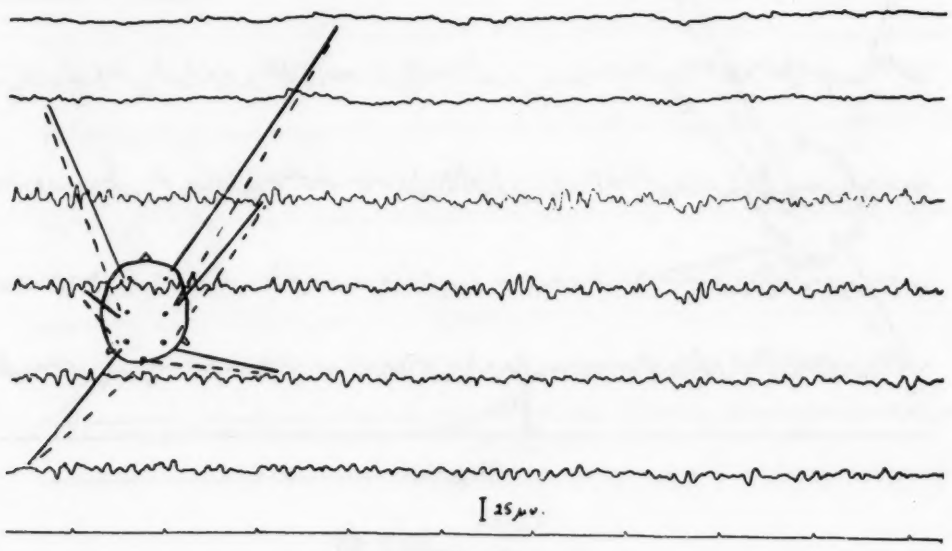

Fig. 13

Case H. 13.

F. A.

Post-partum haemorrhage in 1937 when 36 years old.

Clinically — a mild case.

17 Ketosteroids — 0.69 mg./day.

Basal Metabolic Rate — minus 21 per cent.

18.2.54.

EEG — There was a well developed 9 c/sec. alpha rhythm, a good deal of theta activity with an amplitude up to 30 μV. and also some delta activity.

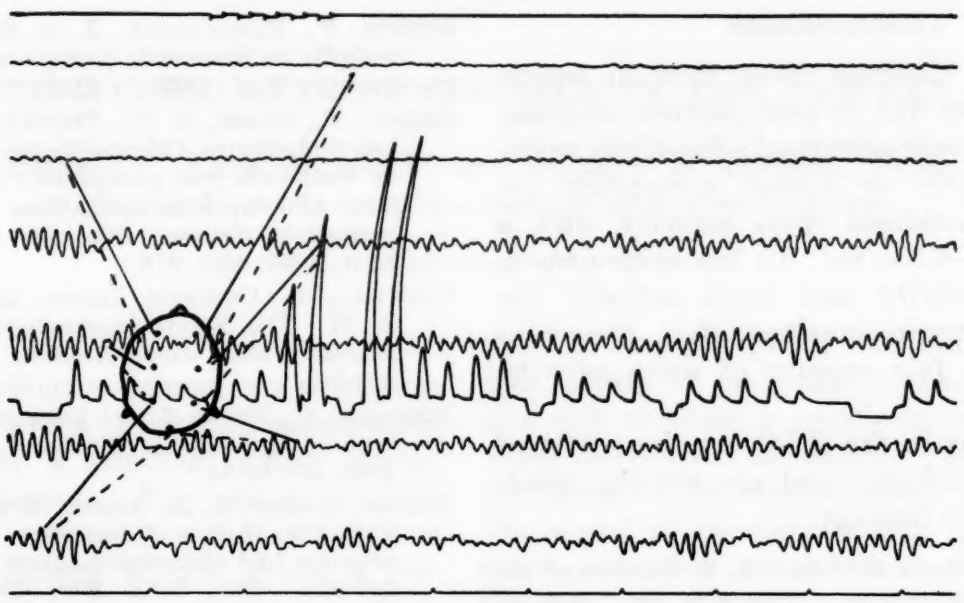

Fig. 14

Case H. 14.

E. G. (33 years).

Severe antepartum haemorrhage in April 1954. recovery slow delayed by collapse of lung and pelvic infection.

Clinically — amenorrhoea, but genitals not grossly atrophic; feels the cold, tires easily, mentally alert; body temperature low.

Basal Metabolic Rate — minus 53. —64 and —44 per cent.

17 Ketosteroids — 1.6 mg. in 24 hours.

26.10.54.

EEG — There was a well developed 8-9 c/sec. alpha rhythm, a fair amount of 7 c/sec. theta activity and a little irregular delta activity.

4.11.54.

EEG — Unchanged.

DISCUSSION

The above series of records demonstrates that there are marked changes in the electroencephalogram associated with hypopituitarism.

In cases 1 to 10 the hypopituitarism was severe; the records in these cases showed that the alpha rhythm was completely or almost completely abolished and was replaced by a theta rhythm with a frequency of 4 to 6 c/sec. (in cases 6 and 7 the frequency was 6.5 c/sec.) with an amplitude varying from 30 to 60 μV. This theta activity was generalised, its amplitude was greatest over the posterior parts of the hemispheres although in a few cases where the theta activity was of considerable amplitude it was well marked in the frontal regions. As a rule the theta activity became somewhat irregular during and after overbreathing; in the cases where delta activity was present in the resting record this was increased during overbreathing and in a few instances was very prominent. In a few instances the theta activity was much diminished or abolished during mental activity.

In the remaining four cases (cases 11-14) the EEG was abnormal but the abnormality was not so marked as in the severe cases. In case 11 the condition was only moderately severe, there was a very considerable improvement on treatment with hormones and the EEG was first done after this improvement had taken place. The record showed a good deal of alpha activity. Cases 12-14 were all clinically mild and had not had any effective endocrine therapy. In case 12 there was a very low amplitude theta rhythm, in cases 13 and 14 there was a good deal of normal alpha activity in addition to the theta activity. It should be noted that in case 14 the record was taken only 6 months after the haemorrhage. The proportion of delta activity in these records may have been under-estimated since the time-constant of the recording system was only 0.1 sec. which would attenuate a 3 c/sec. signal by at least 10 per cent.

CONCLUSIONS

The above findings show that in severe hypopituitarism due to post-partum necrosis, the EEG is grossly abnormal; the alpha activity is completely or almost completely replaced by generalised theta activity with a frequency of 4-6.5 c/sec. In less severe cases, both alpha activity and theta activity are found on electroencephalography. Occasionally there is a fair amount of delta activity also.

The changes in the EEG are the result of endocrine disturbance and are not the result of organic brain damage.

We wish to thank Professor H. L. Sheehan of the Department of Pathology, University of Liverpool for his very considerable help with this work; also Dr. E. T. Baker Bates, Dr. Cynthia Discome and Dr. E. Wyn Jones who have referred certain of these cases to us for investigation. We also acknowledge our indebtedness to the Research Committee of the Board of Governors of the United Liverpool Hospitals for funds to cover certain aspects of this investigation.

REFERENCES

CLARK, E. C., FRANKLIN, M. and SAHS, A. L. Post-partum necroses of adenohypophysis with hypoglycemic convulsions. *Arch. Neurol. Psychiat.*, Chicago, **1951**, *65*: 724-731.

GUINET, P., FAVRE-GILLY, J. et GIRARD, P. F. La maladie de Simmonds post-puerperal. *Rev. Lyonnaise de Med.*, **1952**, *1*: 21-32.

GUINET, P., GARIN, J. P., VERNEY, R. et TARDY, J. Les indications thérapeutiques dans la maladie de Simmonds post-puerpérale: syndrome de Sheeman (Therapeutic indications in post-puerperal Simmonds disease; Sheeman syndrome). *Lyon Med.*, **1953**, *189*: 218.

HOFFMAN, W. CHRISTIE, LEWIS, R. A. and THORN, G. W. The Electroencephalogram in Addison's Disease. *Bull. John Hopkins Hosp.*, **1942**, *70*: 335-361.

MEANS, J. H., HERTZ, S. and LERMAN, J. The pituitary type of myxoedema. *Trans. Assoc. Amer. Phys.*, **1940**, *55*: 32-54.

PIAGGIO-BLANCO, R. A., AUSST, E. G., ACHARD, L. P., CANABAL, E. J. and DIGHIERO, J. Electroencephalogram and electrocardiogram in pituitary myxoedema. *Arch. Urug. Med. Cir. Esp.*, **1950**, *37*: 167-182.

SHEEHAN, H. L. Simmonds disease due to post-partum necroses of the anterior pituitary. *Quarterly Jour. Med.*, **1939**, *8*: 277-309.

SHEEHAN, H. L. and SUMMERS, V. K. The syndrome of hypopituitarism. *Quart. J. Med.*, **1949**, *18*: 319-378.

SIMMONDS, M. Ueber hypophysisschwund mit todlichern Ausgang. *Deutsche Med. Wchnschr.*, **1914**, *40*: 322.

THORN, G. W., FORSHAM, P. H. FRAWLEY, T. F., WILSON, D. L., RENOLD, A. E., FREDRICKSON, D. S. and JENKINS, D. Advances in the diagnosis and treatment of adrenal insufficiency. *Amer. J. Med.*, **1951**, *10*: 595-611.

Reference: HUGHES, ROBERT R. and SUMMERS, V. K. Changes in the electroencephalogram associated with hypopituitarism due to post-partum necrosis. *EEG Clin. Neurophysiol.*, **1956**, *8*: 87-96.

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OPTOKINETIC AFTERNYSTAGMUS IN THE MONKEY [1]

HOWARD P. KRIEGER, M.D.[2] and MORRIS B. BENDER, M.D.
Neurologic Service of the Mount Sinai Hospital, New York City

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INTRODUCTION

Optokinetic afternystagmus is a repetitive eye movement which appears immediately after removal of a stimulus which evokes optokinetic nystagmus. For example, upon cessation of the recurrent optic stimulation created by a revolving striped drum, a few nystagmoid jerks called optokinetic afternystagmus may persist for 1 or 2 seconds. Such afternystagmus, noted in the rabbit, cat, dog and monkey by Rademaker and ter Braak (1948) and in man by Fox, Couch and Dodge (1931) has heretofore been found too transient for analysis. This paper will describe persistent optokinetic afternystagmus in the monkey. The prolongation was effected by recording the after response in the dark.

MATERIAL AND METHODS

Eighteen normal Macaca mulata each weighing 2-3 kg. were studied. They were examined on 71 occasions and optokinetic afternystagmus was found in every instance.

To evoke optokinetic nystagmus the monkey is placed within a cylinder, the inner surface of which consists of vertical black stripes alternating with white spaces. This cylinder, which is 36 inches in diameter and 24 inches in height, is constructed of Moldrite, a white translucent plastic with a matte surface. At intervals of 13¼ inches along the inside surface of the cylinder there are black stripes of 1 inch in width and as high as the drum itself. In all, there are 8 black stripes which appear as figures against a white background. The top of the cylinder is closed by a darkly stained piece of wood which has a source of illumination at its exact center, thereby evenly lighting the inner surface of this drum at any given horizontal level although creating a relatively small gradient along its height. An outside rim drive allows the drum to be rotated about its long axis. The speed of rotation is kept constant by a servo-controlled motor which can turn the drum in both directions at any speed up to 60 revolutions per min.

The monkey is seated in a box which keeps the head straight forward and slightly dorsiflexed. This box is placed inside the cylinder along the center of rotation in such a way that the monkey's field of vision is entirely filled by the inner surface of the drum. The source of light is directly overhead and, therefore, is invisible and does not project a shadow into the field of vision.

Eye movements are recorded with an electroencephalograph by measuring changes in the resting corneo-retinal potential produced by the turning of the eye balls. The technique used is similar to that described for man (Bergman, Nathanson and Bender 1951). The electrodes are 7 phonograph needles inserted intradermally, viz., one just lateral to each outer canthus, one on the bridge of the nose midway between the inner canthi, one at the midpoint of each infra-orbital ridge. This electrode arrangement allows the horizontal and vertical vectors of the changes in the corneo-retinal potential of each eye to be recorded independently, the nasal electrode being common for the horizontal vector of each eye. This placement of electrodes does not interfere with the visual field and does not hamper movements of the eyeballs or eyelids, allowing detection of ocular movements with the eyes open or closed.

The rate of stimulation is correlated with the eye movements by fixing a photoelectric cell just outside the drum, the moving black stripes of which intermittently deactivate the

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[2] Fellow, The National Foundation for Infantile Paralysis.

cell which is connected to the electroencephalograph. The cell also allows the presence or absence of light to be recorded in relation to the eye movements. If desired, a time signal may be introduced into one of the channels of the electroencephalograph. The frequency of stimulation is recorded as the number of stripes passing a given point per second.

To evoke the after response, optokinetic nystagmus must first be elicited. Once this is established, the revolving drum is suddenly stopped. The persistence of nystagmus after the drum has stopped is considered optokinetic afternystagmus. This response is measured by the number of beats per unit time, each beat consisting of a slow phase (deviation of the eyeball from the midposition) and a quick phase (return of the eyeball). A typical record will be found in figure 1.

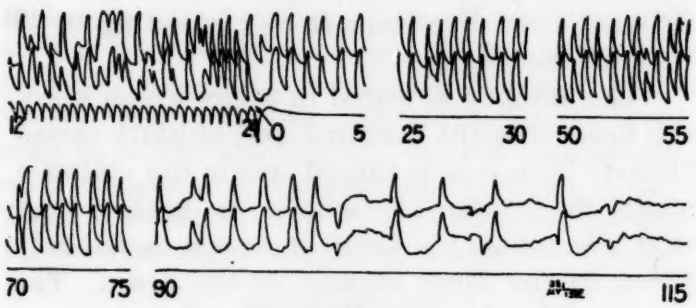

Fig. 1

Typical Optokinetic Afternystagmus

Upper line right eye, middle line left eye, lower line photoelectric cell. In the upper and middle lines gaze to the right is indicated by an upward deflection; gaze to left by a downward deflection. The waves of the lower line indicate the passage of black stripes between the source of illumination inside the drum and the photoelectric cell fixed outside the drum. Inactivity in this line may indicate either total darkness or lack of drum rotation. In all cases recording was at a paper speed of 15 mm/sec.

For purposes of illustration, parts of this particular record are omitted. The numbers below the lower line indicate seconds. Thus, the 12th to 24th sec. of optokinetic stimulation and response are shown. At the 24th sec. the light was extinguished and the drum stopped. Thereafter the eye movements are those of optokinetic afternystagmus. The samples of this response illustrated are from the 0-5th, 25th-30th, 50th-55th, 70th-75th and 90th-115th sec. after the light was turned off. The stimulus was 2 stripes/sec. passing from right to left. The quick phase of both types of response was to the right and the slow phase was to the left.

This technique of recording is applicable to all species including man, where disc electrodes are used instead of needles. Compared to the Dodge camera and infra red photographic methods of recording eye movements the corneo-retinal potential technique has certain advantages. With the latter, the frequency of eye movements may be simultaneously recorded in all planes for both eyes at once whether opened or closed. A graphic record is immediately available and requires neither direct observation of, nor interference with the subject's eye movements or vision. In studying both optokinetic nystagmus and afternystagmus the quick and slow phases (the direction of nystagmus) are immediately recorded and automatically correlated with the rate of optokinetic stimulation and the presence or absence of illumination. Of significance is that this simple method allows unimpeded movements to be recorded simultaneously from both eyes in absolute darkness.

In addition to frequency, other aspects of eye motion may be measured. It should be stressed, however, that the electronic characteristics of the encephalograph are such that essentially the first derivative of the eyeball movements is recorded. Thus, although an accurate record of the frequency of movements, the occurrence of fast and slow phases and the direction of movement in each eye are recorded, the angular displacement of the eye ball from its midposition can only be estimated. It is for this reason that the amplitude of response is considered only qualitatively.[1]

A few precautions must be observed to achieved a good optokinetic response in animals. The animal must be comfortable and awake. In the case of the monkey this is accomplished by use of a restraining seat and conducting the experiments in a cool and well ventilated room. If the animal becomes drowsy or falls asleep, it can be awakened by pinching its tail.

To study the relationship of the immediately preceding optokinetic response to its afternystagmus, the rate and duration of

[1] The amplitude of the recorded response may be greater in one eye than the other (fig. 2c). This is due to lack of complete return of the eyeballs to the center of the orbits during the quick phase of the nystagmus. Under these conditions, the recorded amplitude of the change in the corneo-retinal potential is smaller in the adducting eye.

rotation of the drum were systematically varied. To note the effect of vision upon the after response, it was recorded in light and darkness. Total darkness was achieved by extinguishing all the lights within a light-proof room. To investigate optokinetic after phenomena in the horizontal plane the monkey was seated in an upright position, while for tests in the vertical plane the monkey was placed on its side.

RESULTS

1. *Occurrence of optokinetic afternystagmus.*

As already noted, the after response was elicited from every monkey provided that it was examined in darkness (fig. 1). These movements, though easy to evoke, were however not found in every trial, possibly because of factors which will be discussed below. In no case was spontaneous nystagmus found by merely placing the monkey within the non-rotating drum whether the light was on or off, and optokinetic afternystagmus was impossible without a preceding optokinetic response. However, at times optokinetic nystagmus underwent intermittent, brief, spontaneous cessation in the face of continued stimulation. Despite such periodic cessation, the after response did appear when the lights were extinguished (fig. 4C). It should also be noted that rotation of the drum did not affect the after response elicited in complete darkness.

2. *Duration of optokinetic afternystagmus.*

Measured with the lights on, afternystagmus lasted about 1-2 sec. (fig. 4B). Measured in darkness under optimal conditions, the after response lasted for as long as 420 sec. Under less favorable conditions this after phenomenon was found to last in the order of 20 to 70 sec. In general, the longer the period of optokinetic stimulation, the longer the after response. However, a qualitative relationship between stimulus period and duration of the after response could not be established because of a number of complicating factors: effect of continuous or intermittent stimulation, the quality of the preceding optokinetic nystagmus, fatigue, sleep, the particular animal tested and the presence or absence of illumination. The effects of these factors will be considered below.

3. *Effects of continuous and intermittent stimulation on optokinetic nystagmus.*

Continuous stimulation evoked optokinetic nystagmus 1 to 10 sec. after the onset of drum rotation. Sometimes this response was initially irregular and occasionally it became intermittent as the recording continued. Regardless of the quality of the optokinetic nystagmus, once it appeared afternystagmus could usually be found by plunging the animal into darkness. If the optokinetic response was regular and continuous for more than 10 sec. it was invariably followed by afternystagmus in every trial in every animal. If the response was intermittent, the after response was variable but could be evoked if the animal was touched soon after the lights were extinguished.[1] Under such conditions the afternystagmus tended to be of shorter duration than that following an uninterrupted optokinetic response.

The effect of repeated, brief optokinetic stimulation was different from that of continuous stimulation. Thus a single 5 sec. period of optokinetic stimulation produced nystagmus but not necessarily afternystagmus. However, repetition of such periods of stimulation always elicited an after response. The duration of afternystagmus so evoked increased markedly the more the animal was periodically stimulated. In table I will be found the results of such repetitive stimulation of 4 representative animals. In these studies. except as noted, the after response was allowed to dissipate before the next period of optokinetic stimulation was begun.

4. *Rate of optokinetic afternystagmus.*

At its onset, the frequency of the beat of the afternystagmus was usually indistinguishable from that of the just preceding optokinetic response (fig. 2A). The latter varied with the rate of optokinetic stimulation within limits. Stimulation with about 3 stripes per sec. induced an optokinetic nystagmus of about 3 beats per sec. (fig. 4C). At slower rates of stimulation, the frequency of the optokinetic response tended to exceed the rate of stimulation (fig. 2A, B, C). At faster rates of stimulation, the beat of the optokinetic

[1] The effect of tactile and auditory stimuli will be discussed below.

nystagmus tended to be slower than the number of stripes per minute which passed through the visual field. Thus about 3 beats per sec. appeared to be the optimum following frequency for the optokinetic response. This was also the most common rate of optokinetic afternystagmus at its onset. At times the frequency of the beat of the after response exceeded the rate of visual stimulation. For example, a stimulus of 1 stripe per sec. excited an optokinetic nystagmus of 1-2 beats per sec. at its onset (fig. 2A).

TABLE I

Animal	Stimulus Rate (c/sec.)	Duration of Stimulus (sec.)	Duration of Optokinetic Afternystagmus (sec.)
Monkey 48	3.3	5	2
		5	0
		5.5	2
		5	1.5
		5.5	2
		5	11.5
Monkey 48	2.2	5	10
		5.5	8
		5.5	420
Monkey 45	2.2	1	0
		2	5
		2	0
		2	0
		2.5	6
		2.5	8
		3	5
		5	10
		4	10
		7	35
Monkey 47	2.5	5	0
		5	2
		4	2
		6	1
		10	43
Monkey 47	2.5	5	2
		14	1
		11	4
		8	4
		13	23
Monkey 44	2.2	14	12
		18	12
		7	10
		13	14
		9	62
		(5 min. rest period)	
		7	10
		5	14
		13	50
		(5 min. rest period)	
		5	27
		5	80

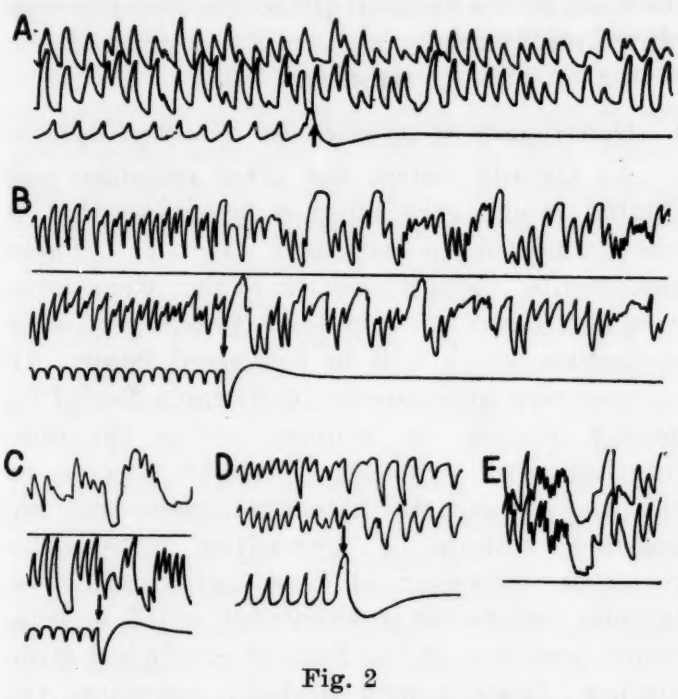

Fig. 2

Variations in the normal pattern of optokinetic afternystagmus

A. Rate of after response of 2 beats/sec., while stimulus was 1 stripe/sec. with an optokinetic response of 1-2 beats/sec. Stimulus: 1 stripe/sec., right to left. Drum stopped and lights out at arrow.

B. Burst of low voltage fast afternystagmus and doubling of response during optokinetic stimulation. Stimulus: 2 stripes/sec., left to right. Drum stopped and light out at arrow.

C. After response faster than optokinetic response with inequality of amplitude of recorded response in right and left eyes. Stimulus: 2 stripes/sec., right to left. Drum stopped and light out at arrow.

D. Afternystagmus slower than optokinetic nystagmus and optokinetic response faster than rate of stimulation. Stimulus: 2 stripes/sec., left to right. Drum stopped and light out at arrow.

E. Section of afternystagmus showing a burst of low voltage, fast activity. In all cases upper, middle and lower lines as in Figure 1.

During the course of the afternystagmus the frequency of the beat declined so that ultimately there was no nystagmus (fig. 1). When the rate of decline was measured as beats per 5 sec. interval, two types of response became apparent: (*a*) if the overall duration of the after response was prolonged, the

initial frequency was maintained and then gradually tapered off in a more or less rectilinear fashion; (*b*) if the overall duration of after response was short, this decline was quasi rectilinear throughout.

At its onset the afternystagmus was regular, i.e. the number of beats per second was about the same. Later, these eye movements often became intermittent, appearing in bursts. Towards its end this nystagmus became irregular, i.e. the number of beats per second was variable and the time between eye movements longer.

The frequency of response also affected the amplitude. As noted above, this was due in part to the electronic characteristics of the recording device but other factors must be involved since at rates of response of 2-4 beats per sec. the amplitude was usually greatest. It was slightly less for faster and slower rates of stimulation, while it was reduced by about 4 times during the bursts of fast optokinetic nystagmus or afternystagmus just described.[1] At the end of these fast bursts, the amplitude as well as the rate each returned to its previous state.

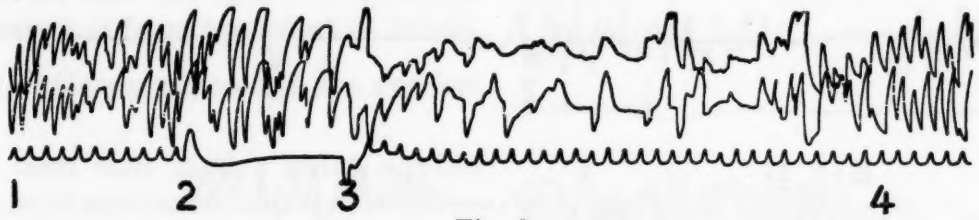

Fig. 3

Effect of afternystagmus upon optokinetic response in the opposite direction

The optokinetic response to left - right drum rotation at 2 stripes/sec. is indicated at 1. At 2 the drum was stopped, the light extinguished and afternystagmus began. At 3 the drum was started in the reverse direction (now right - left) and the light turned on. Gradually the after response with its quick phase to the left (sharp deflection down) was replaced by optokinetic nystagmus with its quick phase to the right (sharp deflection up). The optokinetic response was regular at 4 or about 16 sec. after onset of the reversed stimulus.

Upper, middle and lower lines as in figure 1.

One more observation was made in regard to the frequency of optokinetic afternystagmus. At irregular intervals this frequency suddenly increased to 6-7 beats per sec. (see fig. 2B, 2E, 4A). Such bursts of fast activity lasted for about 1 sec. and were also observed in the optokinetic response.

5. *Amplitude of optokinetic afternystagmus.*

At its onset the amplitude of this afterphenomenon was the same as that of the preceding optokinetic nystagmus (fig. 1, 2A). The amplitude of both responses varied from monkey to monkey, with the placement of the electrodes and with the degree of regularity of the responses. During the stage of decline, the amplitude of the after response fell off but not as rapidly as the rate. Thus the last few beats of afternystagmus, although irregular in occurrence and of relatively slow rate, were of only slightly reduced amplitude (fig. 1).

6. *Direction of optokinetic nystagmus.*

The direction of the quick and slow components of the after response was always the same as its preceding optokinetic nystagmus regardless of how these responses were evoked. It was also observed that afternystagmus in one direction interacted with optokinetic nystagmus in the opposite direction if the former was still in existence. Thus, an after response with a quick component to the right disappeared prematurely and simultaneously delayed the onset of an optokinetic response with its quick component to the left. As noted in figure 3, the jerks in the direction of the afternystagmus gradually dropped out as the newly induced optokinetic nystagmus, beating in the opposite direction, developed belatedly. When the latter became regular no evidence of the after response was visible. Of

[1] Postrotational and postcaloric nystagmus have rates equal to or exceeding optokinetic afternystagmus, with amplitudes which equal or exceed the latter.

course, afternystagmus dissipates in time, but during the experiment just described, it ceased far short of its usual duration.

7. *Effect of darkness on optokinetic afternystagmus.*

Illumination affected both the optokinetic reaction and its afternystagmus. Naturally, optokinetic nystagmus could not be elicited in darkness. In contrast, the after response was best manifested with the lights out. As described above, with the lights on optokinetic afternystagmus was of short duration. It was also of irregular amplitude and frequency. With the lights off, the afternystagmus was much more enduring and regular. The relationship between darkness and the after response was demonstrated in four ways: (1) Once optokinetic nystagmus was established, simultaneously turning off the lights and the drum was attended by the immediate occurrence of a well developed afternystagmus; (2) once the after reaction was established with the lights and drum off, turning on the lights was followed by its almost complete disappearance; (3) if, at this point, the lights were again extinguished, the after response immediately reappeared (fig. 4A); (4) if, once optokinetic nystagmus was established, the drum was turned off but

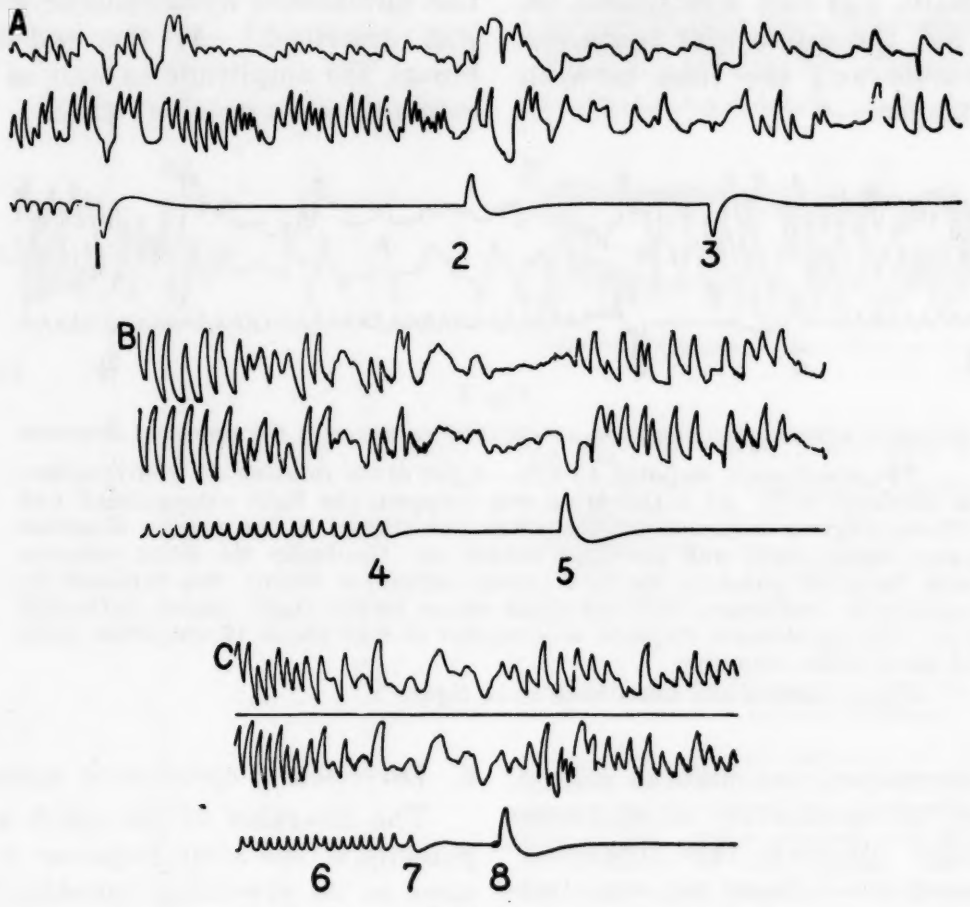

Fig. 4

Effect of illumination on optokinetic afternystagmus

A. At 1 the light was turned off, the drum stopped and the afternystagmus began. At 2 the light was turned on and after response abated. At 3 the light was again extinguished and after response reappeared. Stimulus: 2 stripes/sec., right to left.

B. At 4 the drum was stopped but the light remained on and the after reaction was transient. At 5 the light was turned off and the afternystagmus became manifest. Stimulus: 2 stripes/sec., right to left.

C. Occurrence of afternystagmus despite failure of optokinetic response and interference of light. At 6 the optokinetic response abated spontaneously. At 7 the drum was stopped. At 8 the light was turned off. Stimulus: 3 stripes/sec., right to left.

Upper, middle and lower lines as in figure 1

the illumination remained on, the after response was of poor quality and interrupted by irregular and roving eye movements. However, once this poor after reaction was established, merely turning off the lights changed it to an afternystagmus of good quality (fig. 4B). These relationships between optokinetic afternystagmus and illumination could be demonstrated in all monkeys for as long as this after response would be expected to last had the lights not been turned on once the phenomenon began. Or, in other words, it appeared as if this after phenomenon persisted for a given period and the effect of illumination was to change it from apparent to latent.

8. *Optokinetic afternystagmus in the vertical plane.*

What has been said to this point applies to optokinetic nystagmus and afternystagmus in the horizontal plane. Both types of response were elicited in the vertical plane by placing the monkeys on its side within the drum. There were three significant differences between the horizontal and vertical reactions: (1) the vertical responses were more difficult to evoke than the horizontal; (2) whereas the horizontal reactions were equal to the left and right, the vertical reactions were less apparent when the slow phase was from foot to head or on upward deviation; (3) optokinetic following in the vertical plane was best at a rate of 1 beat per sec. rather than 2.5-3 beats per sec. as in the horizontal plane.

9. *Effect of eyelid closure and non-visual stimuli.*

During these experiments both types of nystagmus occasionally ceased spontaneously. In the case of optokinetic nystagmus this was observed during continued stimulation. In the case of the afternystagmus, the cessation could stop long before it would have been expected to occur in the natural course of events. Such interruption of either type of nystagmus was usually correlated with persistent eyelid closure and not a blink suggesting an association with a condition resembling sleep. Therefore the monkey was pinched or aroused by noise and it was found that such stimuli could lead to the reappearance of either kind of nystagmus (fig. 5).

Both the optokinetic response and after response were also observed to halt under conditions in which there was no eyelid closure. Under these circumstances arousing stimuli, such as pinching of the tail or a loud noise were again effective in reestablishing nystagmus. Although we cannot be certain, it appeared as if the monkey was in a trance or not completely awake during such lapses of the oculomotor reactions. This effect of lack of wakefulness or possibly a lack of

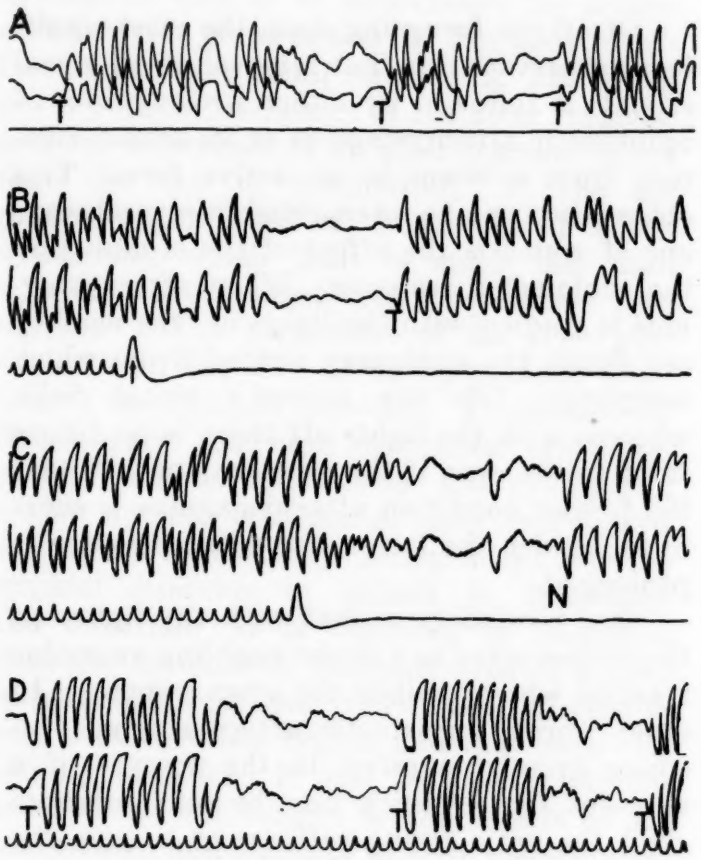

Fig. 5

Effect of non-visual stimuli on optokinetic nystagmus and afternystagmus

A. Afternystagmus repeatedly revived by touching the animal at the points marked T.

B. Revived after reaction faster than after response at its onset. Animal touched at T. Note eyelid EMG indicating closure of eyes during absence of the afternystagmus. Stimulus: 2 stripes/sec., right to left. Drum stopped, light off at arrow.

C. Increase in rate of afternystagmus as animal falls asleep with revival of the after response at a slower rate as a result of making a loud noise at point N. Note eyelid EMG. Stimulus: 2 stripes/sec., left to right. Drum stopped, lights out at arrow.

D. Revival of optokinetic nystagmus by touch when animal falls asleep. Animal touched at point T. Note eyelid EMG. Stimulus: 2 stripes/sec., left to right.

Upper, middle and lower lines as in figure 1.

alertness was also noted in another way. Thus, when at odd intervals optokinetic nystagmus or afternystagmus happened to be irregular, a sudden noise usually reestablished regularity of these eye movements.

DISCUSSION

Of all the foregoing data, the most significant observation is that removal of all visual stimuli is followed by either prolongation of optokinetic afternystagmus or its transformation from a latent to an active form. This observation can be interpreted in several ways one of which is the effect of the stimulus on the oculomotor response. When afternystagmus is studied with the lights on, the monkey can fixate the stationary striped drum which completely fills the animal's visual field, whereas with the lights off there is no figure for fixation even if the eyes are open. Under the former condition afternystagmus is short lived; under the latter, the after response is prolonged.

One possibility is that with the lights on the stripes serve as a target enabling an ocular fixation which inhibits the after response. In other words, optokinetic afternystagmus becomes grossly manifest in the absence of a stimulus figure which may be said either to elicit the optic fixing reflexes or to give the subject something upon which to fix its gaze. The reasonableness of this hypothesis is attested to by the effects of stimuli on related phenomena. For example, both post-rotational and post-caloric nystagmus are enhanced by darkness and diminished by visual stimuli. This hypothesis is also supported by some preliminary observations on the effect of a blinding light (possibly a figureless stimulus) as compared to the effect of the illuminated stationary striped drum on optokinetic afternystagmus. As described, the stationary illuminated drum reduces the duration of the after reaction markedly. The blinding light also reduces the length of this after response but seemingly not as much as the stimulus with dominant figures.

More quantitative data are needed to substantiate the hypothesis of the difference between a figured and figureless stimulus and it is necessary to device a practical figureless stimulus. Nevertheless, the results presented in this study and the observations just offered indicate that the ability of a visual stimulus to suppress or make latent an oculomotor after phenomenon is a fundamental property of the optico-oculomotor cycle.

If it is correct that it is the visual stimuli which suppresses optokinetic afternystagmus, then it would appear that the visual input acts as an inhibitor of the oculomotor after reaction. Such a deduction is not novel, for one of the theories of the proprioceptive control of eye movements (Cogan 1948; Irvine and Ludvigh 1936) maintains that this information is mainly supplied by vision itself, rather than by such proprioceptive mechanisms as may be supplied by the extraocular muscles or by the labyrinthine system. If vision does effect proprioception for eye movements, then darkness would remove this source of sensory input with its inhibitory effect in the alert animal while noise and pain would restore this source of information to the sleepy animal which may be assumed to be "not looking". This last consideration would seem to remove the contradiction that one class of sensory stimuli favors afternystagmus while another inhibits it.

It may be that the relationship between visual stimuli and the visual-oculomotor system is unique, for in contrast to the inhibiting effect of visual stimuli are the enhancing effects of auditory, painful and other "arousing" stimuli on afternystagmus. As noted above, states resembling sleep with or without eyelid closure are associated with a cessation of optokinetic afternystagmus and its after reaction. Both of these responses can be reestablished by auditory or painful cutaneous stimuli. On the surface it appears understandable that the optokinetic response should cease when the lids are closed since the repeated visual stimuli no longer reach the eyes. However, it is puzzling that the afternystagmus stops when the lids are closed but persists when the monkey is in darkness with the lids open. Apparently some factor other than elimination of the visual stimulus is responsible for cessation of eye movements when the eyes are closed in cases of optokinetic, caloric and rotational nystagmus and their respective after effects. Perhaps it is the state of sleep which abolishes the repetitive

response in all of these instances. This hypothesis is suggested by three observations. First, as noted above, the ocular response reappears in the face of an arousing stimulus. Second, during sleep not only are the lids closed but the globes are rolled up and the pupils are constricted. Since this combination of eyelid closure, upward deviation of eyes and pupillary constriction can be obtained on electric stimulation of a specific focus in the brain stem (Bender 1943), it may be that the ocular state during sleep is an active (inhibitory or excitatory) process mediated by a specific system in the brain stem and not just a relaxation of the eyes. It may be this active ocular state during sleep which interferes with nystagmus. Third, recent investigations in this laboratory have led to a proposal of forces which bring the eyes to the midposition, just as there are forces which deviate the eyes laterally or vertically (Bender 1954). Such centering of the eyes may be evoked electrically from wide areas of the cerebrum and the reticular substance of the brain stem (Bender, Teng, Weinstein 1954; Wagman, Werman, and Feldman 1955). There is also clinical and experimental evidence that these eye centering forces may be equated with the quick component of all types of jerky nystagmus and that during natural or induced sleep these centering forces are abolished (Bender 1955). These deductions suggest a possible mechanism (abolition of the centering forces) for the disappearance of optokinetic nystagmus and afternystagmus during sleep. [1]

These relationships between nystagmus and afternystagmus on the one hand and sleep and arousing stimuli on the other, also suggest that the ascending reticular activating system (Magoun 1952) plays a role in these reactions.

Another sensory effect which might be a determinant of optokinetic nystagmus is after imagery. That is, optokinetic stimulation might induce moving after images striking enough to attract attention and provoke afternystagmus when the illumination is extinguished. For the monkey this possibility cannot be excluded. However, moving after images are not formed in humans stimulated by our technique and stationary ones appear in only a few individuals.

Certain other aspects of optokinetic afternystagmus may be of importance for understanding this phenomenon: 1. The additive effect of repeated small stimuli. 2. The apparent optimum frequency of the after response and the occurrence of an after reaction faster than the rate of stimulation. 3. The apparent upper limit of frequency of afternystagmus, which limit is much less than that of post-rotational and post-caloric nystagmus. 4. The persistence of the after phenomenon in the face of an optokinetic stimulus in the opposite direction. These observations suggest that once rhythmical eye movements, such as optokinetic afternystagmus, are set up they continue of their own accord and become relatively independent of the original stimulus in regard to frequency and duration. It is tempting to postulate that the optokinetic stimulus creates a corresponding repetitive, rhythmical discharge within the nervous system and that once this activity is evoked it also becomes relatively autonomous but subject to the effects of visual stimuli and states of altered wakefulness. Here it should be recalled that in rabbits Rademaker and ter Braak (*op. cit.*) elicited nystagmus in the dark with a single light passing across the visual field.

The persistence of repetitive rhythmical activity within the nervous system is a well known phenomenon and has been variously explained (Hill 1933; Lorente de Nó 1938; Lloyd 1949; Pitts, Magoun and Ranson, 1939; Pitts 1946; Adrian 1931; Forbes 1922; Jasper 1936; Frank *et al.* 1948). Whether any of these explanations can be applied to optokinetic afternystagmus is problematic. The question is whether this after response is an inherent rhythm which can be made apparent under certain conditions of examination or whether it is an imposed activity which subsides faster under some conditions than others. An investigation of the anatomic and physiologic details of this after response with particular attention to the role of the

[1] It should be noted that natural or induced sleep also abolishes other rhythmic movements such as tremors and choreas (Wechsler 1947).

pertinent internuncial neuronal chains of the brain stem will be needed to answer this question.

SUMMARY

Optokinetic nystagmus and its afternystagmus was studied by recording of corneoretinal potential with the electroencephalograph. This technique registers eye movements in light and dark, binocularly and uniocularly, with the eyes opened or closed, and does not interfere with the field of vision or the range of eye movement.

Optokinetic afternystagmus is readily elicited from the monkey provided it is examined in darkness. The direction of these eye movements is determined by the antecedent optokinetic stimulus. The frequency and duration are only partially determined by this stimulus. Optokinetic afternystagmus is diminished and in time obliterated by light, but it may be brought out again by returning the animal to darkness thereby demonstrating that light merely makes the phenomenon latent and does not abolish it. This after response is suppressed by eyelid closure and sleep and can be reestablished by waking the animal. These observations may be analyzed in many ways, e.g. figure-ground relationships of the stimulus, the effect of sleep on eye movements, proprioceptive mechanisms, internuncial neuronal pools of reciprocating forces, but a definitive mechanism has yet to be worked out.

REFERENCES

ADRIAN, E. O. Potential changes in the isolated nervous system of Dysticus Marginalis. *J. Physiol.*, **1931**, *72*: 132-151.

BENDER, M. B. Eyelid closure reaction. *Arch. Ophthal.*, **1943**, *29*: 435-444.

BENDER, M. B. The eye centering system (A theoretical consideration). *A.M.A. Arch. Neurol. Psychiat.*, **1955**, *73*: 685-699.

BENDER, M. B., TENG, P. and WEINSTEIN, E. A. Centering of eyes. *A.M.A. Arch. Neurol. Psychiat.*, **1954**, *72*: 282-295.

BERGMAN, P. S., NATHANSON, M. and BENDER, M. B. Electrical recordings of normal and abnormal eye movements. *Trans. Amer. Neurol. Assoc.*, **1951**, *76*: 232.

COGAN, D. G. *Neurology of the Ocular Muscles.* Charles C. Thomas, **1948**, Springfield, Ill., p. 23.

FORBES, A. The interpretation of spinal reflexes in terms of present knowledge of nervous conduction. *Physiol. Rev.*, **1922**, *2*: 361-414.

FOX, J. C., COUCH, F. H. and DODGE, R. Optic nystagmus. *Arch. Neurol. Psychiat.*, Chicago, **1931**, *26*: 23-25.

FRANK, L. K., HUTCHINSON, G. E., LIVINGSTON, W. K., MCCULLOCH, W. S. and WIENER, N. Teleologic mechanisms. *Ann. N. Y. Acad. Sci.*, **1948**, *50*: 187-277.

HILL, A. V. *Cold Spring Harb. Symp. Quant. Biol.*, **1933**, *1*: 146-151.

IRVINE, S. R. and LUDVIGH, E. J. Is ocular proprioceptive sense concerned in vision? *Arch. Ophthal.*, **1936**, *15*: 1037-1039.

JASPER, H. H. Cortical excitatory state and synchronism in the control of bioelectric autonomous rhythms. *Cold Spring Harb. Symp. Quant. Biol.*, **1936**, *4*: 320-338.

LLOYD, D. C. Functional organization of the spinal cord. *J. Neurophysiol.*, **1941**, *4*: 184-190.

LLOYD, D. C. Post-tetanic potentials of presynaptic actions in the spinal cord. *Fed. Proc. Amer. Soc. Exp. Biol.*, **1941**, *8*: 99.

LORENTE DE NÓ, R. Analysis of the activity of chains of internuncial neurons. *J. Physiol.*, **1938**, *1*: 207-244.

MAGOUN, H. W. The ascending reticular activating system. *Res. Publ. Ass. nerv. ment. Dis.*, **1952**, *30*: 480-492.

PITTS, R. F. Organization of the respiratory center. *Physiol. Rev.*, **1946**, *26*: 609-630.

PITTS, R. F., MAGOUN, H. W. and RANSON, S. W. The origin of respiratory rhythmicity. *Amer. J. Physiol.*, **1939**, *127*: 654-670.

RADEMAKER, G. C. J. and TER BRAAK, J. W. G. On the central mechanism of some optic reactions. *Brain*, **1948**, *71*: 48-74.

WAGMAN, I. H., WERMAN, R. and FELDMAN, D. S. Cerebral pathways for conjugate eye deviation and centering. *Fed. Proc.*, **1955**, *14*: 162.

WECHSLER, I. S. *Textbook of Neurology.* W. B. Saunders Co., Philadelphia, Pa., 6th Edit., **1947**, p. 586.

Reference: KRIEGER, H. P. and BENDER, MORRIS, B. Optokinetic afternystagmus in the monkey. *EEG Clin. Neurophysiol.*, **1956**, *8*: 97-106.

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STUDIES OF CEREBRAL CIRCULATION IN BRAIN INJURY

III. — Cerebral contusion, laceration and brain stem injury [1]

JOHN S. MEYER, M.D.

Neurological Unit, Boston City Hospital and the Department of Neurology, Harvard Medical School, Cambridge, Mass.

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INTRODUCTION

In a previous study of experimental cerebral concussion evidence was presented that the first effect of cerebral trauma is local transient paralysis of neurones (Meyer and Denny-Brown 1955). In a study of a large series of penetrating and closed head injuries in man, carried out by the United States Navy, it was evident that early focal and diffuse reduction in EEG activity may be followed in a short period of time by diffuse or focal high voltage slow activity. Since the traumatic stimulus was of brief duration it appeared probable that these delayed changes in the electrical activity of the brain were related to circulatory and metabolic disturbances. This possibility was of particular interest because it is at the time of maximal EEG abnormality that early focal epilepsy may transiently appear. Such early epilepsy is known to bear no significant relation to the incidence of post-traumatic epilepsy. It was also apparent that patients with acute brain injury were particularly susceptible to oxygen lack and alteration of water balance (Caveness, W. F., unpublished observations).

In the hope of gaining additional data in relation to any circulatory or metabolic changes we have studied brain contusion, laceration, herniation and brain stem injury in the experimental animal.

METHODS

Observations have been made on the monkey (Macacus rhesus) and cat. Records are available on 22 contusions, 12 lacerations, 3 fatal brain stem injuries and 2 penetrating wounds. The effects of varying degrees of change in intracranial pressure have been studied in 20 experiments, with numerous examples of brain herniation and compression ischemia of the brain stem.

Records were made of cortical oxygen availability, temperature and pH together with respirations, blood pressure, EKG and EEG. In some experiments concurrent records were made of cortical injury potentials (S.P.) intracranial pressure and jugular venous pressure. These recording methods have been described and their validity discussed in a previous communication (Meyer and Denny-Brown 1955).

Contusion was produced by striking the exposed cortex sharply with a small stainless steel hammer having a striking surface diameter of one centimeter. This method permits study of bordering changes after contusion. Another method has been to increase the extradural pressure rapidly .causing the exposed brain in another area to suddenly strike the edge of a trephine hole. This method, using light weight electrodes, permits study of the changes in the center of the bruised zone.

Laceration was made by abrasing the pia arachnoid and its superficial vessels with a sharp hook or knife.

Brain stem contusion was made by an excessively severe blow with either the percussion or compression concussion apparatus described in a previous study (Meyer 1955). The former consists of a weight dropped onto a column of saline on the exposed dura. The latter consists of a saline filled metal syringe screwed into the skull the plunger of which is struck by a hammer. Contusion of the brain stem was demonstrated at necropsy.

[1] This study was supported by a research grant from the United States Navy.

Opinions expressed are those of the author and do not necessarily represent those of the Department of the Navy.

Brain stem compression (ischemia) was caused by progressively increasing the extradural pressure by continued pressure of several seconds duration on the plunger of the syringe.

Brain herniation was caused by gradually increasing the extradural pressure for several minutes with an area of cortex exposed through a trephine hole. This area gradually becomes congested. Similar brain herniation was also caused by injecting saline into the cisterna magna under pressure.

Penetrating wounds were made by allowing the weight of the percussion concussion apparatus to fall directly through the exposed cortex of the occipital lobe from a height of 4 feet 6 inches.

RESULTS

Cerebral contusion results in a visible bruising of the brain without subarachnoid hemorrhage. Immediately after the blow the area swells, becomes visibly red, and then progressively purple over the next 2 or 3 min. This purple color appears at necropsy to be due to clusters of small hemorrhages in gray and adjacent subcortical white matter. The hemorrhages take 1 to 3 min. to develop and the intracranial pressure shows a fluctuant rise with their development (Denny-Brown and Russel 1941).

Brain contusion is associated with a negative S.P. potential arising from the area injured. This potential is different in some respects from the rapidly reversible surface negative change seen with concussion. Since contusion is more obvious in white matter the exploring S.P. electrode was placed in this region to sample the maximum area of injury. The reference electrode was put in an area of cortex remote from the injured area. The white matter in the contused area becomes negative with respect to the area of uninjured cortex, showing a rapid initial negativity, then a fluctuating increase and decrease followed within a few minutes by a slow irregular return to the steady state during from 5 to 15 min. or longer depending upon the severity of the injury (fig. 4). The fluctuant period before returning to the steady state corresponds closely with the development of petechial hemorrhages and is presumably due to them. This type of white matter injury potential is the opposite of the surface negativity seen in concussion (Meyer and Denny-Brown 1955).

The EEG in severe local cerebral contusion uncomplicated by brain stem injury shows only local effects. They may be first diminished amplitude activity during the concussive phase, followed by progressively higher amplitude slow activity in the 2-6 c/sec. range. In some instances slow activity may predominate from the moment of injury. Local bursts of fast activity and intermittent spike activity are common later particularly if local or light anesthesia is used. This spike activity appears to arise only from the injured region (fig. 5) and has only shown evidence of spread in one experiment in this study. Spikes usually appear after a latency of 1 to 30 min. or longer. Similar patterns of EEG activity were found by Glaser *et al.* in experimental studies of local pressure effects on the brain. In their study seizure activity occurred in 85 per cent and of these seizures 95 per cent were localized to the pressure electrodes (Glaser and Sjaardema 1946). This method of brain injury is more likely to result in severe local ischemia. In the present study EEG seizure activity appeared in 8 of 22 contusions.

Cerebral contusion results in a local progressive cerebral hypoxia, which in mild contusion is reversible but in severe contusion is not. A moderate contusion as in figure 1B, insufficient to cause a rise in blood pressure caused local, transient diminished EEG activity, a rise followed by a rapid fall within 12 sec. of the bordering EPG, and an immediate fall in the EPG in the region of injury. The cortical temperature in the injured area fell steadily. After 2½ min. the local temperature and oxygen electrodes returned to the steady state but were still at a reduced level. The C.S.F. pressure slowly fell to control readings at the same time. The EEG during the hypoxic phase showed focal moderate voltage slow wave activity.

Gradual application of extradural pressure equivalent to 20 mm. of water (fig. 1A), compressing the cortex against the trephine hole, but insufficiently rapid to cause con-

tusion results in a rise in jugular venous pressure, a slight rise in blood pressure, a few gasping respirations and a transient reversible fall in the cortical oxygen potentials. The cortical temperature showed a minimal rise. The fall in oxygen availability and rise in cortical temperature appears to be due to local stagnant anoxia from compression of cortical veins.

Figure 1C shows the bordering changes around a contusion caused by striking the exposed cortex with a hammer. A temperature electrode (T) just within the visible area of petechial hemorrhages begins to fall after a latent period of 48 sec. and then falls progressively. The bordering EPG electrode shows an early fall with a rhythmic rise as the collateral circulation increases. The EPG oxygen electrodes remotely removed on the occipital and frontal poles show essentially no change except those reflecting change in blood pressure and respiration. The EEG showed local occipital spike activity in the same area where the temperature electrode showed diminished blood flow and the EPG fluctuant hypoxia as cortical petechial hemorrhages appeared.

Following cortical contusion there is an acid pH shift of gradual development in the contused zone reaching a maximum after 2 min. when a more or less complete return to the steady state may occur (fig. 6). This confirms the observation of Sonnenschein *et al.* 1953, that an area of injured brain becomes acid. The more severe the contusion the more severe the acid shift and the slower and less complete the resolution. With a small stab wound the acid shift is only 0.1 pH units but with a heavy contusion the acid shift may amount to 0.5 pH units and may persist for

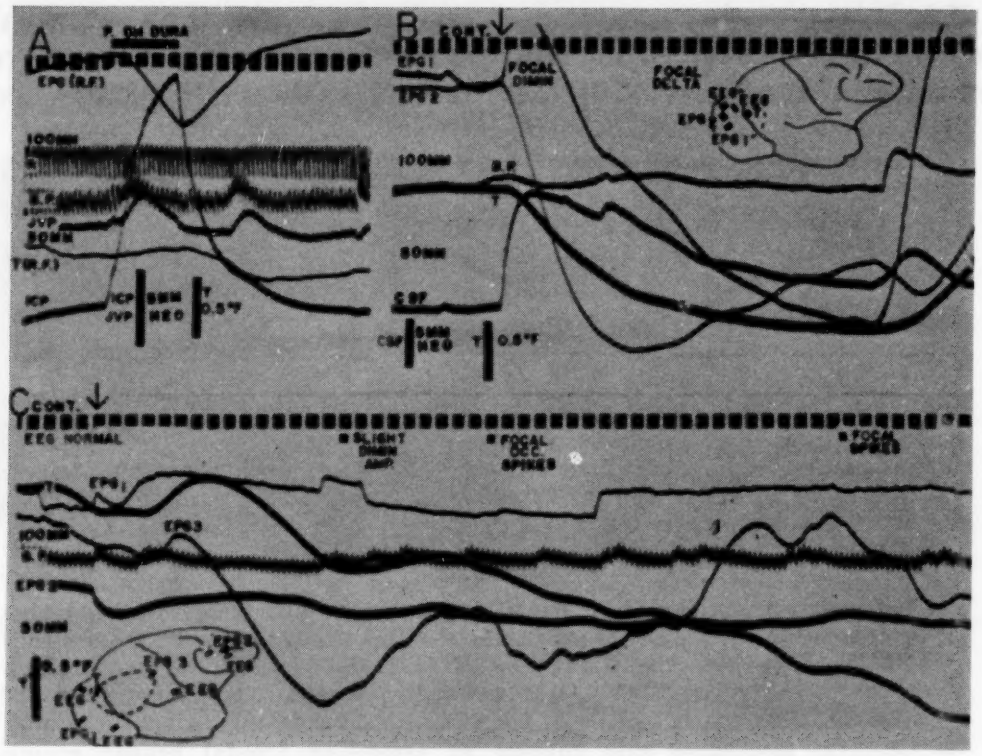

Fig. 1

A. Effect of slowly progressive extradural pressure with cerebral compression. The intracranial pressure rises higher than jugular venous pressure. There is a gradual mild hypoxia from venous stasis. Time marked in 6 sec. intervals at top of record.

B. Brain contusion by suddenly expanding the brain against trephine hole (broken line). Severe local ischemia and hypoxia with incomplete recovery. EEG first locally diminished then local delta.

C. Bordering changes of a contused zone (broken line) caused by striking cortex. EPG 3 and T lie just within the uninjured zone. Delayed appearance of local spikes in EEG.

15 min. before a slight return to alkalinity begins. The acid shift in a zone of contusion probably accounts in part for the bordering hyperemia, together with the local tissue hypoxia. A similar relationship of bordering hyperemia and local acidity has been seen following vascular occlusion in another series of experiments.

In a severely contused zone there is a progressive, persistent acid pH shift, fall in local temperature and oxygen availability. The maximum fall we have encountered is 0.7 pH units, 1.5 degrees F. in temperature and 75 per cent of the EPG fall seen with breathing pure nitrogen for 45 sec. The fact that the EPG in a contused zone still shows a diminished, sluggish response to occlusion of the common carotid arteries and nitrogen breathing in the injured zone indicates that circulation is still present within the zone but severely impaired.

We have recorded the EPG oxygen levels in a contused zone for several hours. Such prolonged recording is technically difficult because the general condition of the animal may deteriorate and the blood pressure fall. However, in the center of a severely contused zone a slowly progressive hypoxia may continue for as long as 3 hours, tending to stabilize at a low level. The damaged cortex at this time was visibly swollen but not totally ischemic, such as is seen in cerebral infarction (Denny-Brown *et al.* 1954).

If there is associated with the contusion a large increase in intracranial pressure, then the blood pressure shows an enormous rise due to brain stem compression and ischemia. The cortical oxygen availability as well as the temperature may show a rise in the early congestive phase associated with the rise in blood pressure and possibly the local concussive effects. The EEG shows slow activity during this period but eventually within 1 to 3 min., an hypoxic phase develops probably related to the development of petechial hemorrhages and visibly associated with brain swelling, with a fall in cortical temperature, oxygen availability and pH. It has also been shown in these experiments that the occipital EEG response to light flashes on the retina with a stroboscope may still be elicited a few minutes after a contusion of the anterior occipital region. A fall in the cortical oxygen availability occurs as is seen prior to injury but the temperature fails to show a compensatory rise and the oxygen availability continues at low levels for several minutes after cessation of the stimulus. In one experiment (fig. 5) in which focal paroxysmal EEG activity occurred in the occipital region after

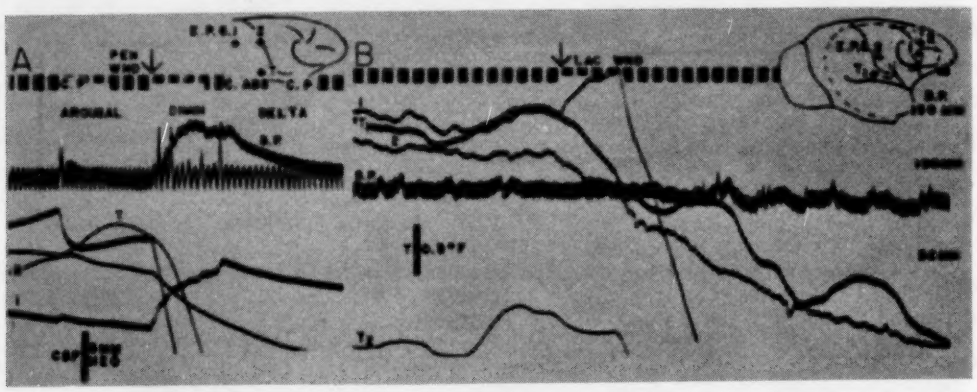

Fig. 2

A. Penetrating wound caused by 70 gram weight dropped 4 feet 6 inches on exposed cortex. Inspite of a large rise in blood pressure, diminished EEG and loss of corneal reflexes, EPG 1 and 2 and T electrodes show severe fall resulting from large cerebral contusion. EEG shows delayed delta activity.

B. Cerebral laceration with rupture of ascending frontal branch middle cerebral artery. Ischemia and hypoxia in distribution of main trunk of middle cerebral artery due to spasm and blood loss. Time marked in 6 sec. intervals.

a contusion the effect of light flashes were tested during the recovery phase from the seizures, the frequency of the spike activity was increased during the light flashes but causal relationship to the stimulus could not be established as the discharge continued unabated when the stimulus was removed.

Cerebral laceration. By the term laceration we imply interruption of the continuity of the brain surface, as by tear or rupture. Such a wound results in subarachnoid hemorrhage as well as local contusion. In figure 2B, a lacerating wound with a tear of the ascending frontal branch of the middle cerebral artery resulted in subarachnoid hemorrhage. There is a fall in all temperature and oxygen electrodes, including those in the distribution of the sylvian branch of the middle cerebral artery. This sudden reduction of local cortical blood flow and oxygen reservoir was accompanied by some fluctuations in blood pressure but the ischemia is partially reversible. When active bleeding ceased after the event illustrated in figure 2B the electrodes began to rise after approximately 5 min. but did not reach control levels. It is probable that this severe fall, in relation to vessels considerably beyond the distribution of the ruptured vessel, is due to a combination of reduction in the local head of arterial pressure by blood loss and to arterial spasm.

On the other hand small stab wounds without hemorrhage or vessel injury caused by pricking the intervascular space with a needle or Von Graefe knife produced no remarkable effects on EPG electrodes located 5 mm.

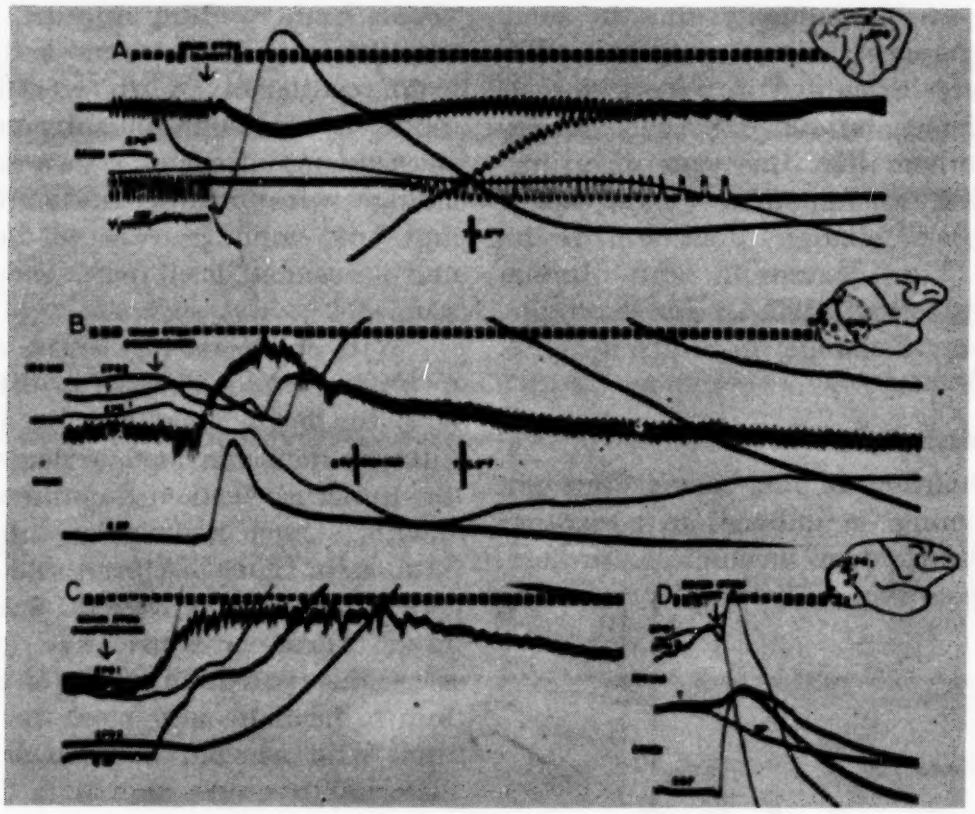

Fig. 3

A. Brain stem contusion and death caused by excessive blow with comp. conc. apparatus. Brain herniation at tentorium and foramen magnum with fall in CSF pressure followed by rise. Respiration shows delayed failure with resultant cerebral hypoxia and eventual vasomotor collapse.
B. and C. Two examples of brain stem compression and ischemia caused by progressive extradural pressure. There is an enormous rise in blood pressure with resultant cerebral hyperemia. Extradural pressure in C was longer in duration than B.
D. Fatal brain stem contusion by sudden injection of saline in cisterna magna. There is vasomotor collapse with resultant cerebral ischemia and hypoxia. Time marked in 6 sec. intervals.

distant in the cortex although an adjacent cortico-cortical S.P. electrode showed a significant rapidly reversible S.P. shift. Such an injury is known to effect the permeability of blood vessels in the area injured (Broman 1949) suggesting that endothelial permeability may be impaired unassociated with remarkable changes in local oxygen availability. The S.P. changes are similar to those reported in spreading depression produced by a similar stimulus and are presumably due to some propagated traumatic injury potential. We have not directly attempted to record spread of such disturbance, but our experience agrees with that of others that this type of injury potential is not accompanied by sufficient vascular or hypoxic change to account for its propagation (Van Harreveld and Stamm 1952; Freygang *et al.* 1954). For example, there is no delayed change in electrode EPG 2 in figure 1C.

Cerebral herniation and brain stem injury.

When herniation of the cortex through a trephine opening is induced in a manner that avoids brain stem herniation through the foramen magnum, as by slowly injecting

Fig. 4

Monkey, Nembutal anesthesia. Graph of the injury potential (S.P.) in millivolts of the white matter near a contused zone with respect to uninjured cortex. Contusion signaled by arrow. Calibration of millivoltmeter readings shown to left of record. Time intervals are 30 sec.

saline into the cisterna magna, there is initially a stage of venous congestion with a slow fall of local cortical oxygen availability and a slight increase or no change in cortical temperature in the affected zone (fig. 1A). The cortical pH shows an initial alkalinity of 0.1 - 0.3 pH units. As the herniation continues the temperature, pH and oxygen electrodes begin to show a fall as the circulation in the herniated cortex is impaired. The pH may fall as much as 0.5 units to the acid side. Evidence that impaired local circulation is the cause of the fall may be shown by the delayed and sluggish response of the EPG electrode to the effect of nitrogen and occlusion of the common carotid arteries compared to an uninjured area.

Prolonged observation of brain herniation for several hours shows that within 5 min. visible brain swelling appears. The degree of local hypoxia is not as marked as with severe brain contusion. With cessation of the stimulus by reducing the intracranial pressure the sequence of events is reversible. The EEG changes with brain herniation are not marked and only mild decrease of local amplitude and occasional local paroxysmal activity are seen.

With an excessively severe concussive blow or with a rapid increase in intracranial pressure the brain stem may be injured and at autopsy petechial hemorrhages are seen in the upper cervical cord and medulla (3 experiments). Such injuries are almost invariably fatal as in figure 3A produced by an excessive blow caused by a weight dropped onto the intact dura, pressure was exerted for 0.4 sec. This caused the brain stem and cerebellum to herniate and block the foramen magnum with associated brain stem injury, the cisternal pressure showed a fall during the phase of block with a rise as the herniation receded. Respirations were arrested for almost 2 min., returned and then failed again, death being due to delayed respiratory failure. Associated with respiratory failure there is a fall in the cortical temperature and oxygen availability. The delayed failure of respiration here is the striking feature and is attributed to the development of hemorrhages in the brain stem. At autopsy multiple petechial hemorrhages were found in the medulla, pons and the second cervical segment of the cord. Similar pathological findings have been reported by others in experimental brain injury (Denny-Brown and Russell 1941).

A similar picture may be seen with a sudden increase of intracranial pressure by a rapid injection of saline in the cisterna magna (fig. 3D). This was accompanied by visible

herniation of the brain at the skull defect. The blood pressure fell as did the cortical temperature and oxygen availability of the cortex. Large amplitude slow waves in the EEG appeared first in the area of herniated brain at the time of the severe fall in oxygen tension.

Gradual increase in the extradural pressure with reversible brain stem compression and resultant ischemia (20 experiments) produced initially the opposite effect of brain stem injury. The vasomotor center is stimulated by ischemia with a resultant enormous rise in the blood pressure (the Cushing effect). The EPGs and cortical temperature passively following the rise (fig. 3B and C). The fall in EPG 1 in figure 3B is believed to be due to local cortical compression by the edge of a trephine hole. A similar rise in blood pressure is seen with brain stem ischemia resulting from occlusion of the vertebral arteries (Meyer and Denny-Brown 1955).

In one experiment a severe blow was accompanied by the development of bilateral epidural hematomas and we were able to witness the sequence of brain stem ischemia and injury resulting from continued brain stem compression. The blood pressure first rose and then fell precipitiously.

In a small animal it is difficult to produce contusion and herniation of cerebral cortex without associated medullary effects. With injuries to a larger brain, as in man, such medullary effects are less common.

Effects of decompression. When a severe increase of intracranial pressure results in

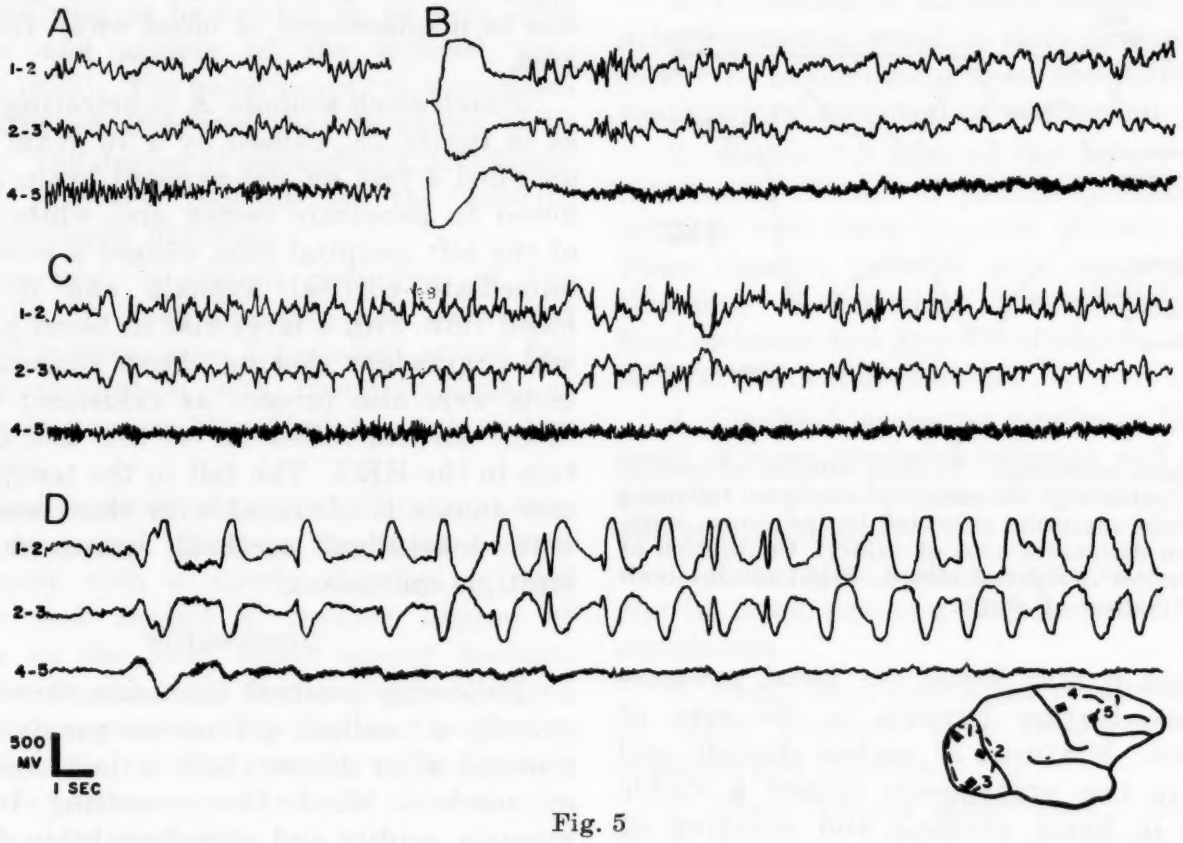

Fig. 5

Monkey, local Procaine anesthesia. Electrocorticogram in cerebral contusion. Cortex outlined by interrupted line was rapidly compressed against the edge of the trephine hole by extradural pressure. Electrode placement shown in diagram.
A. Control record prior to injury.
B. Immediately after injury.
C. One min. after injury occipital spike activity begins in contused anterior occipital region. This continued for one min. and then subsided.
D. Nine min. later a second paroxysm of spike and slow activity begins.
The oxygen availability and cortical temperature in injured zone showed a progressive fall for 40 sec. after injury. The intracranial pressure showed a secondary rise 40 sec. after the injury.

brain herniation, impaired local circulation and local hypoxia, any measure that tends to lower intracranial pressure appears to be beneficial. Reduction of the intracranial pressure by the aspiration of cerebrospinal fluid or widening the skull defect results in improved cortical oxygen availability. The administration of hypertonic glucose (50 per cent) solution is occasionally transiently beneficial but it may lower the blood pressure and cause further hypoxia in the area of herniation. Mixtures of carbon dioxide and oxygen in two experiments caused a visible increase in brain swelling and lowering of cortical oxygen availability attributed to further cerebral congestion and raised venous pressure.

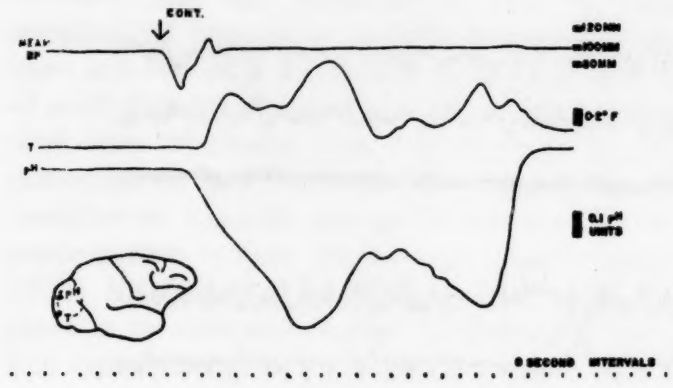

Fig. 6

Monkey, local anesthesia. To show relation of cortical pH and bordering temperature changes following occipital lobe contusion indicated by the arrow, interrupted line designates area of injury. Calibration of each parameter to right of record. Eight sec. intervals marked at bottom of graph.

Relation to venous pressure. Cerebral contusion and brain herniation are associated with a marked rise in the jugular and intracranial pressures which are greater than occur in concussion. The rise in intracranial pressure precedes and exceeds that of jugular venous pressure presumably because local compensation in intracranial pressure is made by displacement of venous blood. Thus any maneuver which raises venous pressure is deleterious to the compensation mechanism (Meyer and Denny-Brown 1955).

The effect of distortion of the brain without compression has been further studied by suddenly causing a weak negative pressure of several seconds duration in the epidural space on the side of the skull opposite the trephine opening. Intracranial pressure recorded from the opposite hemisphere showed a negative pressure of 5-10 mm. of mercury. No significant alteration resulted in blood pressure, respirations, EEG, S.P. or corneal reflex but a definite transient slow fall in the cortical oxygen availability occurs in the opposite hemisphere which is thought to be due to displacement of blood away from this area.

Penetrating wounds. A penetrating wound as in figure 2A, caused by a 70 gram weight dropped 4 feet on the exposed brain and allowed to penetrate cortex and white matter of the left occipital lobe, caused a severe and immediate cortical hypoxia and decreased blood flow with a large rise in blood pressure and respiratory slowing. Some concussive effects were also present as evidenced by loss of the corneal reflex for 48 sec. and diminution in the EEG. The fall in the temperature and anoxia is identical with those associated with generalized cerebral compression and multiple contusions.

DISCUSSION

Following cerebral contusion there is frequently a localized percussion paralysis complicated after 45 sec. with a local reduction in cerebral blood flow resulting in local hypoxia, acidity and secondary brain damage. The time course of these changes, together with the fluctuant negativity in local S.P. potential prior to the return to the steady state, suggests that the development of petechial hemorrhages and vascular injury is the cause of the reduction in local blood flow. Some of the EEG changes can also be closely related to this sequence of events. In the concussive phase there is reduction of electrical activity, in the ischemic phase there is frequently local slow wave and spike activity. However, our evidence does not exclude the possibility that direct neuronal injury may also give rise to EEG abnormalities. In local brain compression local seizure activity appears with remarkable regularity (Glaser and Sjaardema 1946) so that this complication may well be related to local circulatory effects.

Local vascular insufficiency in brain contusion is severe but not absolute as in cerebral infarction produced by the venous distension method (Denny-Brown *et al.* 1954). It is comparable to infarction caused by occlusion of a branch of the middle cerebral artery (Meyer *et al.* 1954). On the edge of the contused zone compensatory increases in the collateral circulation appear similar to those seen in vascular occlusion and appear from other evidence to be related in part to local hypoxia and acidity of the injured area (Meyer 1955). The blood supply to a contused zone, although impaired, may be shown to be present. The degree of impairment, and therefore of recovery, depends on the severity of the traumatic stimulus.

In cortical laceration reduction of the local head of blood pressure and associated spasm of vessels cause a transient severe fall in local circulation with tissue hypoxia, as the bleeding ceases the effect is more or less reversible.

Brain herniation shows two distinct phases, first a congested phase as the veins become compressed with a slowly developing mild hypoxia and second a further degree of hypoxia as the local blood supply becomes critically impaired. At this stage the damaged area becomes swollen. The degree of vascular impairment in the early stages of brain herniation is seldom as severe as in contusion and is usually reversible.

Brain stem ischemia produced by herniation at the foramen magnum manifests itself by a rise in blood pressure and a resultant cerebral hyperemia. Brain stem contusion shows the opposite effect, a delayed failure of respiratory and vasomotor centers with the rapid onset of cerebral ischemia and hypoxia.

In a previous study (Meyer 1955) we have offered evidence that the same type of neuronal injury underlying the general disturbance called concussion can be restricted to the immediate locale of injury. It is then still a reversible neuronal paralysis without anatomical correlate. In the present paper we have examined the effects of more severe restricted injuries of various kinds and find the sequence of events altered according to whether contusion and/or laceration is added to the picture.

CONCLUSIONS

1. Experimental cerebral contusion, laceration, herniation and brain stem injury have been studied in terms of local cortical oxygen availability, blood flow, and pH together with local EEG, S.P., respiratory and blood pressure changes.

2. Contusion of the brain results in a local injury potential which is more prolonged and slower in development than the diffuse neuronal injury potential of concussion.

3. Within 1-3 min. of the injury causing contusion evidence of localized impaired circulation and tissue hypoxia become evident. These changes coincide with the visible development of petechial hemorrhages. Such local ischemic and hypoxic changes may result in local EEG abnormalities.

4. Cerebral laceration results in the rapid onset of more extensive ischemia and hypoxia due to local reduction of arterial pressure and arterial spasm.

5. Brain stem ischemia results in a severe rise in blood pressure and increased cortical circulation.

6. Brain stem contusion results in a fall in blood pressure with resultant cerebral ischemia and hypoxia.

7. Brain trauma causes first a local transient paralysis of neurones complicated in later stages by the effects of ischemia, anoxia and resulting metabolic disturbances. In contusion these secondary effects overshadow the paralytic effects.

REFERENCES

BROMAN, T. Permeability of the cerebrospinal vessels in normal and pathological conditions. *Ejnar Munksgaard Forlag*, Copenhagen, **1949**, 92 pp.

CAVENESS, W. F. Unpublished observations.

DENNY-BROWN, D., FANG, H. C. and HORENSTEIN, S. A polarographic study of cerebral infarcts produced by venous distention. *Trans. Amer. Neurol. Ass.*, **1954**, 46-49.

DENNY-BROWN, D. and RUSSEL, W. R. Experimental cerebral concussion. *Brain*, **1941**, *64*: 93-164.

FREYGANG, W. H. JR., LANDAU, W. M. and MARSHALL, W. H. Changes in resistance and electrical potential in the cortex. *Fed. Proc.*, **1954**, *13*: 48.

GLASER, M. A. and SJAARDEMA, H. M. Effect on the electroencephalogram of localized pressure on the brain. *J. Neurophysiol.*, **1946**, *9*: 63-72.

MEYER, J. S. and DENNY-BROWN, D. Studies of cerebral circulation in brain injury. I. Validity of combined local cerebral electropolarography, thermometry and steady potentials as an indication of local circulation and functional changes. *EEG Clin. Neurophysiol.*, **1955**, *7*: 511-528.

MEYER, J. S. and DENNY-BROWN, D. Studies of cerebral circulation in brain injury. II. Cerebral concussion. *EEG Clin. Neurophysiol.*, **1955**, *7*: 529-544.

MEYER, J. S., FANG, H. C. and DENNY-BROWN, D. Polarographic study of cerebral collateral circulation. *Arch. Neurol. Psychiat.*, Chicago, **1954**, *72*: 296-312.

SONNENSCHEIN, R. R., WALKER, R. M. and STEIN, S. N. A microglass electrode for continuous recording of brain pH *in situ*. *Rev. Sci. Instruments*, **1953**, *24*: 702-704.

VAN HARREVELD, A. and STAMM, J. S. Vascular concomitants of spreading depression. *J. Neurophysiol.*, **1952**, *15*: 487-496.

Reference: MEYER, JOHN S. Studies of cerebral circulation in brain injury. III. Cerebral contusion, laceration and brain stem injury. *EEG Clin. Neurophysiol.*, **1956**, *8*: 107-116.

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CENTRAL RETICULAR PATH TO INTRALAMINAR AND RETICULAR NUCLEI OF THALAMUS FOR ACTIVATING EEG RELATED TO CONSCIOUSNESS [1]

JAMES W. PAPEZ, M.D.
Laboratory for Biological Research, Columbus State Hospital, Ohio
and Department of Mental Hygiene and Corrections, Ohio

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Nerve impulses of a non-specific nature reach the cerebral cortex when alpha rhythms are recorded. They are associated with a general state of consciousness. Activation of the alpha rhythms is known to be in the reticular formation of the oblongata, pons, and midbrain from where it is distributed to the cortex by the thalamic reticular system of nuclei and fibers. The activation of cortical EEG by this brain stem formation was described by Moruzzi and Magoun in 1949. Jasper (1949) found that the thalamic reticular system produced not only the non-specific activation of the cortex but also influenced activation of specific nuclei of thalamus and related sensory areas in the cortex. There was interaction between the non-specific system and sensory systems. This integrative action of thalamocortical mechanisms was amplified by Jasper and Ajmone-Marsan (1950) and by others. The intralaminar nuclei send fibers to the reticular nucleus on the outer surface of the thalamus. Together they form the organized thalamic reticular system. The reticular nucleus in turn transmits these impulses to all parts of the cortex as demonstrated by Hanbery, Ajmone-Marsan and Dilworth (1954), and the foregoing authors.

The special function of the intralaminar nuclei has come into prominence because they serve to conduct non-specific impulses to the cortex which evoke EEG rhythms, arouse and alert the individual. These impulses were shown to be a function separate from that of the specific sensory nuclei of the thalamus as shown by Jasper (1949), and Hanbery and Jasper (1953).

Purpose of this paper is to illustrate fiber connections of the intralaminar and reticular nuclei from a study of series of sections of human brain stems. It is an attempt to define the anatomic paths and to show their relations to recent EEG findings of others. The pattern of fibers between the intralaminar and reticular nuclei was found to agree with EEG experiments (Starzl and Magoun 1951; Hanbery, Ajmone-Marsan and Dilworth 1954). I shall try to show how this path of fibers is derived from an early evolution of thalamic nuclei in the reptiles (Papez 1935).

Reticular formation of the oblongata and pontine tegmentum is a primitive, diffuse system of interlacing fibers among nerve cells. It forms the central core of each half of the brain stem. It is bordered by nuclei of origin or termination of fifth to twelfth cranial nerves whose many special connections contribute to its reticular structure. These nerve connections are bilateral and concerned with vital, internal processes such as seeking, breathing, feeding, circulation and related bodily adjustments and attitudes.

Correlation of cranial nerve impulses is the significant function of the reticular formation. The resultant actions are often composite ones. Impulses from stomach and other abdominal viscera, from heart, lungs, larynx and pharynx come chiefly by way of the vagal nerves. The glossopharyngeal nerves bring impulses from the pharynx and taste buds of the tongue. The motor connections of these nerves regulate visceral activities including respiration (Pitts 1946). Trigeminal nerves bring impulses from the face, mouth, nose, sinuses, orbits and dura mater. Their motor fibers are concerned with chewing, enunciation, etc. Together the functions of the fifth, seventh and twelfth cranial

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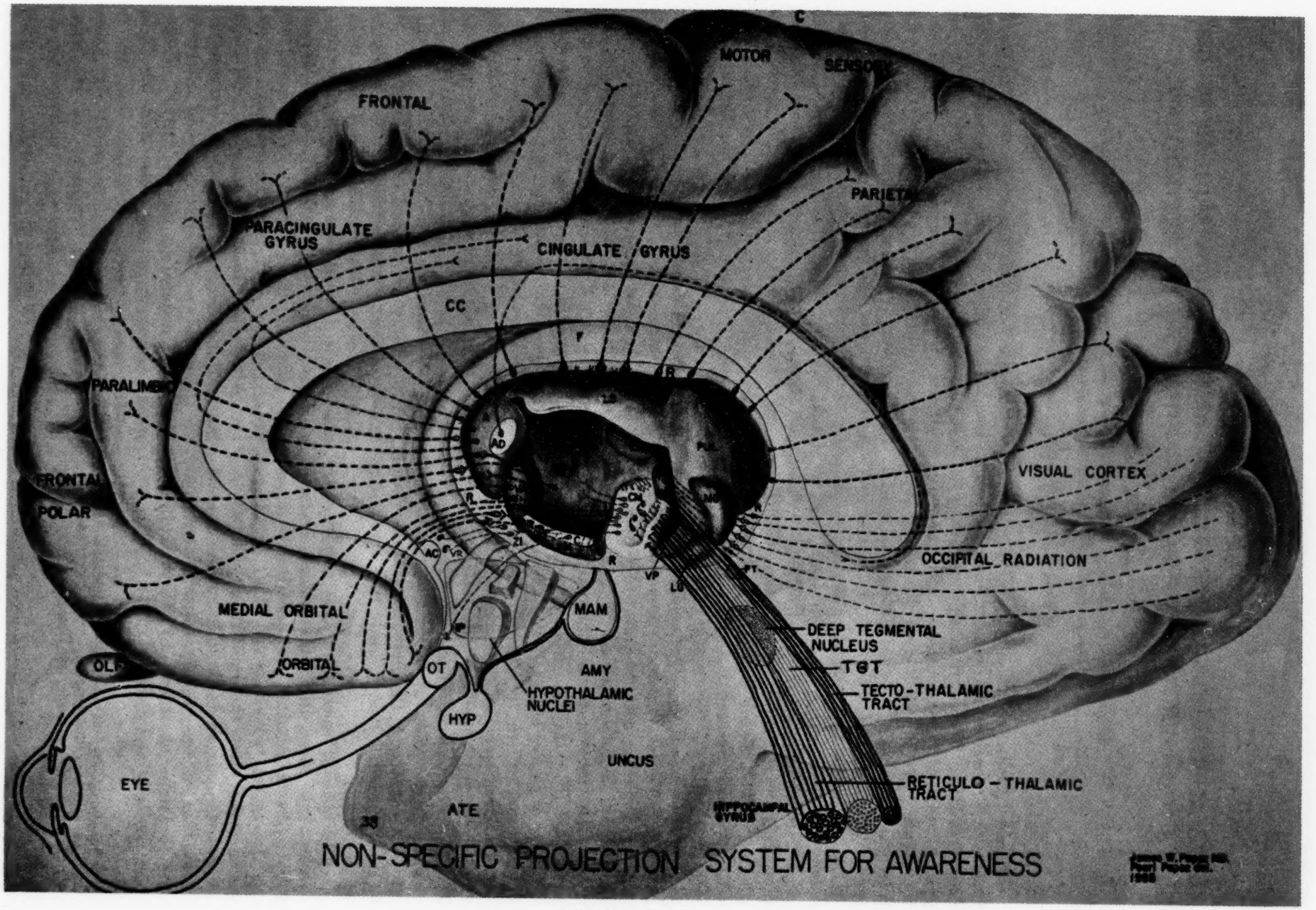
Read before Society of Biological Psychiatry, Chicago, Ill. June 1955.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NON-SPECIFIC PROJECTION SYSTEM FOR AWARENESS

nerves are correlated in a complex series of actions in mastication, swallowing and speech. The vestibular nerves regulate functions of tonus, posture and equilibrium. Cochlear nerves transmit impulses from vibrations which activate the cochlea. A more ancient vibration system persits in the parabigeminal nucleus and tectothalamic tract seen in the tegmental formation of the midbrain.

Ascending paths from the reticular formation are mainly three. The fasciculus tegmenti dorsolateralis or reticulothalamic tract RTT (fig. 1, 2) is continuous from the bulbar region to the centrum medianum (Singer and Yakovlev 1954; Russell 1954). To its lateral side are the lemniscal systems which contribute collaterals to the deep tegmental nucleus of the midbrain DT where the other tegmentothalamic tract is formed TGT. Impulses of the reticular activating system have been traced along both of these paths by Magoun (1952) and others. The tectothalamic tract TT is lateral to the others.

Tegmentum of the midbrain is a broad area of cells and fibers situated ventral to the optic tectum (fig. 2). Its medial portion is formed by the reticulothalamic tract RTT and the rubroreticular tract combined to form a common bundle. Its lateral part is occupied by a formation of fibers among scattered nerve cells which form the tegmentothalamic tract TGT. On its lateral side is the small, compact tectothalamic tract TT which passes by the ventral pretectal nucleus PT. These tegmental structures are surrounded on their ventral side by the medial lemniscus and trigeminothalamic tract, on their lateral side by the spinothalamic tract ST, and on their dorsal side by the pretectal nucleus PT and fibers of the tectopontine tract, not shown in figure 2. Collaterals from these large fiber tracts, and fibers from the reticular tract and superior colliculus or tectum enter the deep tegmental nucleus in TGT.

Deep tegmental nucleus receives fibers ascending from the reticular formation, from the tectum and from the central gray as well as the collaterals mentioned above. It sends a bundle of fibers to the subthalamic nucleus of Luys. This nucleus in turn sends the subthalamic (supramamillary) decussation to the prerubral nucleus (fig. 4, PR) of the other side (Papez 1940). Stimulation of the deep tegmental nucleus produced emotional attitudes (Weinstein and Bender 1947). The evoked movements seemed to have bodily and optic components. Corticotegmental fibers coming from the basal regions of the forebrain enter this tegmental region.

Ventral pretectal nucleus PT is also called the posterior nucleus of the thalamus (Papez and Aronson 1934). It is large and ventral in lower mammals as in rabbit and cat where it receives strong connections from the optic tract. It sends fibers under the red nucleus to the laterally bent peduncle of the substantia nigra. The tectothalamic tract TT makes connections with the pretectal nucleus on its way to the nucleus limitans L. In birds the lateral spiriform nucleus seems to have connections similar to the ventral pretectal nucleus of mammals PT.

Tegmentothalamic connections (Johnson 1953) are mainly four: (*a*) fibers of the reticulothalamic tract RTT pass over the red nucleus to reach the centrum medianum CM and parafascicular nucleus PF. There they end radiating into these nuclear masses in a lateral and dorsal direction (fig. 3). In the primates the nuclei are large, displaced and crowded against the pretectal region and medial dorsal nucleus MD. This made study of sections difficult; (*b*) at the end of the

Fig. 1

Path of projection of non-specific impulses related to EEG and consciousness passing to the right thalamus and cerebral hemisphere. Reticulothalamic RTT and tegmentothalamic TGT tracts end in intralaminar nuclei, centrum medianum CM, parafascicular PF, and limitans L which send fibers to reticular nucleus R, thence to occipital cortex. Intralaminar bundle I goes to submedial SM, paracentral PC and central lateral CL which connect with reticular R, thence to temporal and parietal cortex. Submedial SM sends inferior thalamic peduncle IP to anterior perforated substance NB and amygdala. Ventral medial VM, ventral anterior VA and reticular R in front send fibers to orbital and frontal cortex. Anterior nucleus A sends fibers to cingulate gyrus. Cortical connections are shown in figure 8.

reticulothalamic tract some of its ventral fibers end in the narrow subfascicular nucleus SF. This obscure region may, with some uncertainty, be considered a gustatory station in the thalamus (Kuhlenbeck 1954). In Weigert sections, the nucleus is a clear area; (*c*) the tegmentothalamic fibers coming from the deep tegmental nucleus of the midbrain also end in the centrum medianum and adjacent cells; (*d*) the tectothalamic tract comes from the tectum and in part from an old static or vibration center, the parabigeminal nucleus situated ventral to the inferior colliculus and adjacent to the nucleus of the lateral lemniscus (fig. 2 TT). The tract ascends in a lateral position, lodged in the dorsal border of the spinothalamic tract ST. It contacts the pretectal nucleus PT and turns dorsally to end in the nucleus limitans L and some large cells dorsal to the centrum medianum allied to the paracentral nucleus PC.

Other less well known fibers enter the centrum medianum (Papez 1940, p. 44). Some fibers come from the ventral part of the medial geniculate nucleus and pass across to end in the centrum medianum. They represent an ancient tractus tectoreuniens of reptiles (Papez 1936). A small terminal of the brachium conjunctivum turns up from the red nucleus (Papez 1940). It is distinct in carnivora. One may infer that these minor tracts contribute impulses to the intralaminar nuclei.

Intralaminar nuclei occupy the internal medullary lamina of the thalamus. They include centrum medianum, parafascicular, limitans, central, paracentral and central lateral (Papez and Aronson 1934, Walker 1938, Droogleever-Fortuyn and Stefens 1951 and others). To these the submedial and ventral medial are joined by intralaminar fibers I. The large cells of the medial dorsal nucleus MD close to the internal medullary lamina are also involved.

Parafascicular nucleus PF surrounds the habenulointerpeduncular tract medial to the centrum medianum (fig. 3). It receives the medial dorsal fibers of the reticulothalamic tract. It sends fibers laterally to the reticular nucleus R which in turn sends fibers to the occipital cortex (fig. 1).

Nucleus limitans or lentiformis L is situated at the medial border of the pulvinar at its junction with the tectum (Kuhlenbeck 1954). Its relation to the dorsal division of the brachium or superior colliculus is intimate. It seems probable that its fibers arise in the nucleus limitans and pass out to the reticular nucleus R. The polarity of this dorsal bundle is uncertain and should be investigated, since occipital alpha rhythms may be concerned. Afferent connections to nucleus limitans seem to come from the neighboring pretectal nucleus and the tectothalamic tract. This is a confused region where optic fibers cross ascending fibers which curve dorsally. The tectothalamic fibers contact the pretectal nucleus and curve dorsally to the limitans. Fibers from the suprageniculate nucleus (fig. 2, SG) and spinothalamic tract swing in the same direction. The ventral pretectal or posterior thalamic nucleus PT is situated posterior to the centrum medianum into which it seems to send many fibers. A large pretectonigral bundle curves ventrally to the peduncle of the substantia nigra. The connections of the pretectal nucleus are seen best in the rabbit, sheep and cat. They are already well defined in reptiles (Papez 1935, 1936) and are prominent in birds.

Centrum medianum is a large oval cellular mass in the posterior end of the thalamus (fig. 3, CM). This nucleus receives the bulk of fibers of the ascending reticulothalamic tract RTT and also tegmentothalamic fibers TGT coming from the deep tegmental nucleus. As the fibers come to the level of the centrum medianum they turn laterally and disperse as fine neuropil among the cells of the nucleus. Fibers from the large cells of the centrum medianum pass ventrally and out to the reticular nucleus R, from which fibers pass into the internal capsule presumably going to the temporooccipital cortex for alpha rhythms.

Small granule cells G in the lateral part of the centrum medianum receive fibers from the lateral regions of the dorsal thalamus and possibly also from the putamen (Rundles and Papez 1937). These probably inhibit alpha rhythms. There is evidence that granule cells of the periventricular region also inhibit non-

specific rhythms (Kaada 1951). Posterior paraventricular granule cells extend from massa intermedia to habenula.

Intralaminar bundle of fibers arises from other cells of the centrum medianum (fig. 4, I). It is a broad band of myelinated fibers with some nerve cells in its medial part (Papez 1940, pp. 43-44). Fibers from these cells pass ventrally and out to the lower part of the reticular nucleus R which sends fibers into the internal capsule going presumably to the lower frontoparietal cortex. I in figure 4 stands for fibers and cells.

The intralaminar bundle passes forward where its fibers end in the central C, submedial SM, ventral medial VM, and paracentral PC nuclei. These nuclei occupy the internal medullary lamina along a level passing through the massa intermedia C, and forward.

Central nucleus (fig. 4 and 5, C) is close to the midline and extends into the massa intermedia. The latter is the thalamic commissure for a minor bilateral exchange of nonspecific impulses. Fibers that pass through the massa intermedia come from the bordering intralaminar nuclei as well as from centrum medianum and periventricular cells further back (Papez 1940). Bilateral integration of activating impulses probably takes place in reticular formation of brain stem.

Paracentral nucleus PC sends fibers upward along the internal medullary lamina to the central lateral nucleus CL under the lateral dorsal nucleus LD.

Central lateral nucleus receives fibers from the intralaminar bundle and from the paracentral nucleus. It sends fibers out under the lateral dorsal nucleus and over the lateral anterior nucleus LA to end in the upper margin of the reticular nucleus R. From the reticular nucleus fibers enter the internal capsule and go presumably to the dorsal cortex of the upper frontoparietal region of the brain.

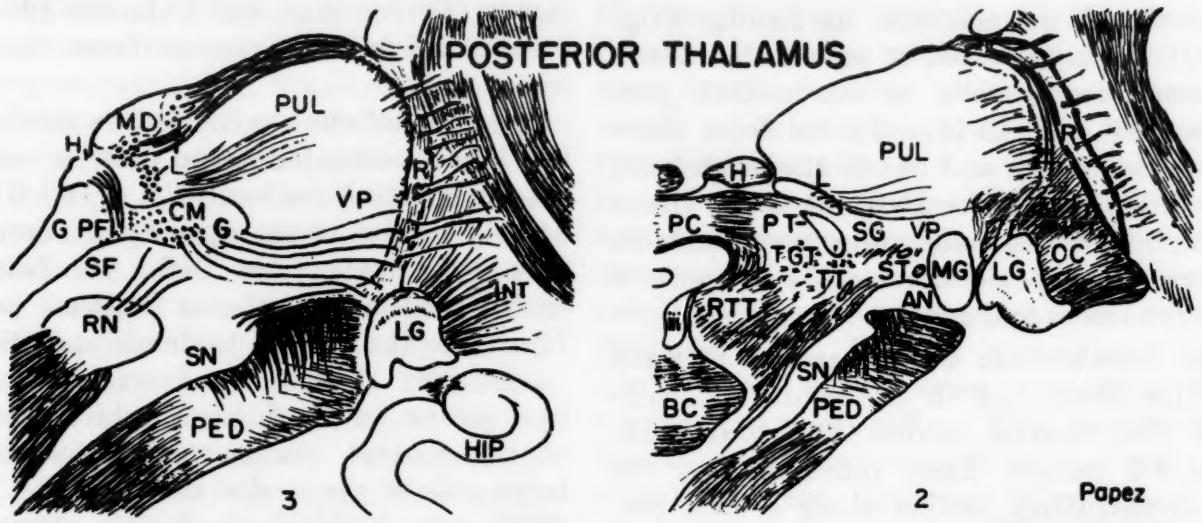
Medial dorsal nucleus MD in its medial and ventral parts which border on the paracentral nucleus, has cells larger than elsewhere (fig. 4, arrow). Fibers from these cells join those from the paracentral PC and submedius SM and pass ventrally as the inferior thalamic peduncle (fig. 7, IP). Other fibers from these nuclei enter the frontal thalamic radiation FR and are distributed to the medial, orbital, insular and inferior frontal cortex (Levine 1944, and Yakovlev 1954). The frontopontine tract arises from this same cortex.

Submedial nucleus SM (often labeled VM) is a large triangular group of cells ventral to the paracentral nucleus (fig. 5 and 6). It is usually medial to the upgoing portion of the mamillothalamic tract MT. Its fibers are contributed to the inferior thalamic peduncle IP and to the frontal thalamic radiation FR.

Inferior thalamic peduncle (fig. 6 IP) is a strong band of fibers which comes out of the central, paracentral, submedial and large cells of the medial dorsal nuclei (Papez 1940, and Kuhlenbeck 1954). Because of absence of neuropil, one gets the impression that the peduncle rises in these nuclei, and gets some fibers from the anterior nucleus near-by. The peduncle passes ventrally, inclines forward and turns laterally into the anterior perforated substance where its identity is lost around the nucleus basalis NB. From here the amygdalar tract AT passes laterally to the central nuclei of the amygdala, and also the olfactohabenular tract passes dorsally to the habenular nuclei. Stimulation of amygdalar efferents causes sniffing and coughing (Hess and Müller 1934). This suggests that vagal as well as olfactory afferents reach the amygdala. Some of the amygdalar tract fibers pass beyond into the anterior temporal nucleus (fig. 1, ATE) which joins the uncinate cortex to the temporal polar area 38, where visceral and olfactory functions may have a more extended cortical representation. According to Walker (1954) fibers from the parataenial and anterior paraventricular nuclei also follow the inferior thalamic peduncle. A foremost demonstration of the amygdalar functions was that of MacLean (1950).

Frontal thalamic radiation (fig. 7, FR) passes forward to the orbital, insular cortex and inferior frontal gyrus. It comes mainly from the medial dorsal MD, ventral medial VM, ventral anterior VA and frontal part of reticular nucleus R (seen in fig. 6). The anterior nucleus A sends fibers chiefly to the

HUMAN THALAMUS
SECTIONS TO SHOW INTRALAMINAR AND RETICULAR NUCLEI



cingulate gyrus on the medial surface of the brain (fig. 1).

Ventral medial nucleus VM is situated ventral to the submedial in a more anterior position. The two nuclei are closely allied (fig. 6 and 7). Fibers arise from the cells of the ventral medial nucleus and enter the frontal thalamic radiation FR. In front of the inferior thalamic peduncle the radiation passes down and forms the most ventral fibers of the anterior limb of the internal capsule in its course through the striatum where it passes the anterior commissure AC. Traced frontally these fibers curve ventrally through the striatum above the olfactory tubercle. Here they enter the orbital cortex spreading laterally and forward over the orbital cortex. This is an orbital radiation OR. It carries some fine fibers from the reticular nucleus R to this cortex.

Ventral anterior nucleus VA is lateral to the ventral medial. It also contributes a large bundle of fibers to the frontal thalamic radiation of the internal capsule (fig. 6 and 7). This radiation passes to the orbital cortex (fig. 7 FR). Many of its fibers arch over the dorsal margin of the putamen to enter the external capsule and end in the claustrum and insular cortex. It is probable that fibers pass to the frontal and orbital opercula that overhang the insula. The fronto-pontine tract arises from this opercular cortex (Yakovlev 1954). Descending cortico-tegmental tracts have been demonstrated in experimental animals. Fibers in the orbital, insular and amygdalar regions myelinate during the first two months of infancy (Flechsig 1876). Fibers from the frontal part of the reticular nucleus pass to the frontal cortex.

In summary, passing to the medial frontal, orbital, insular, and inferior (opercular) frontal cortex, four sets of fibers diverge from the frontal thalamic radiations: (1) Inferior thalamic peduncle goes to the anterior perforated substance. (2) Fibers from the submedial and ventral medial nuclei go to the orbital cortex. (3) Fibers from the ventral

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Fig. 2

Drawing of frontal half-section of human midbrain at its junction with thalamus. It shows position of ascending reticulothalamic RTT, tegmentothalamic TGT, and tectothalamic TT tracts that end in parafascicular PF in figure 3, centrum medianum CM and limitans L nuclei of figure 3. Connections of limitans L are to reticular nucleus R, thence to occipital cortex. Figures show right half of human thalamus. X2.

Fig. 3

Drawing of section through posterior intralaminar nuclei, parafascicular PF, centrum medianum CM and limitans L, and their connections out to reticular nucleus R, thence fibers into internal capsule. Note connection from red nucleus RN to centrum medianum, and granule cell nuclei G in relation to centrum. X2.

Fig. 4

Drawing of section through middle of thalamus, showing intralaminar band I cut across, to submedial nucleus (in fig. 5) where inferior thalamic peduncle IP takes origin. Paracentral nucleus PC connects out to lower part of reticular R, and central lateral CL sends fibers over LP to upper part of reticular R, from which fibers pass into internal capsule INT. X2.

Fig. 5

Drawing of section in middle of thalamus through massa intermedia C, and submedial nucleus SM which receives the intralaminar bundle I, and sends out inferior thalamic peduncle IP. Paracentral PC and central lateral CL nuclei send fibers over LA to reticular R. thence fibers into internal capsule. Zona incerta ZI sends fibers into ventral radiation VR to pallidum. X2.

Fig. 6

Drawing of section through anterior thalamus showing anterior nucleus A. Submedial nucleus SM sends inferior thalamic peduncle IP to region of nucleus basalis NB which gives rise to olfacto-habenular tract OH. Fibers may also pass back in IP. Amygdalar tract AT, ventral anterior nucleus VA. X2.

Fig. 7

Drawing of section through front end of thalamus at level of anterior commissure AC and ventral medial nucleus VM and its orbital radiation OR. Frontal radiation FR from ventral anterior nucleus VA. Radiation VR comes from reticular nucleus and zona incerta. X2.

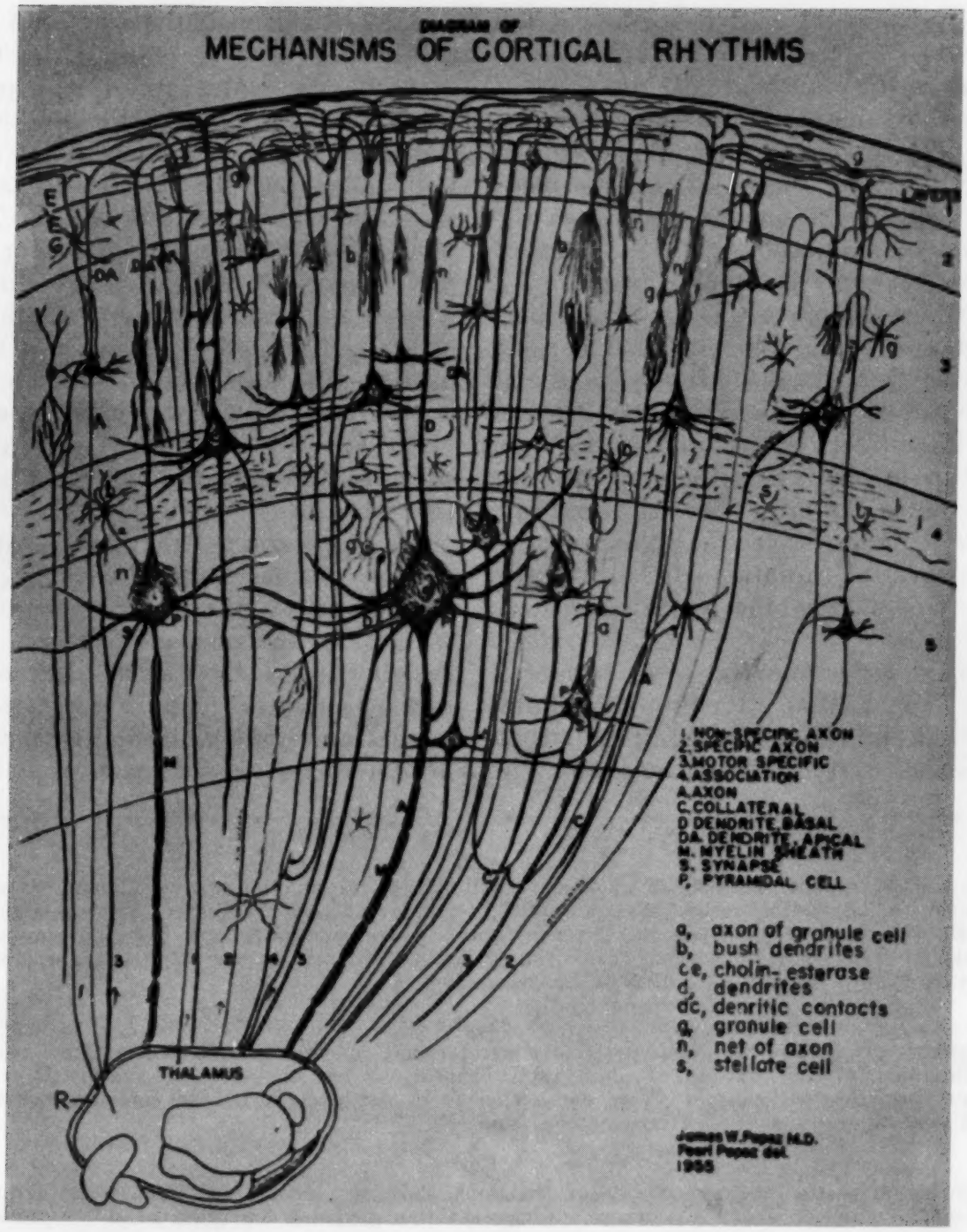

Fig. 8

Drawing of mechanisms of cortical rhythms. Non-specific fibers 1 from reticular nucleus R for EEG synapse on pyramidal cells in upper part of layer 3 and discharge their axons back to thalamus. Their apical dendrites DA back-fire to layer 1 where they contact dendrites of granule cells in layer 2 which discharge their axons into nets they make around pyramidal cells. Typical relations of granule cell nets to pyramids are shown near outer granular layer 2 and inner granular layer 4.

A,	Anterior nucleus	C,	Central nucleus
AC,	Anterior commissure	Cau,	Caudate nucleus
AMY,	Amygdala	CC,	Corpus callosum
AN,	Anterior tegmental nucleus	CL,	Central lateral nucleus
At,	Amygdalar tract	CLA,	Claustrum
ATE,	Anterior temporal nucleus	CM,	Centrum medianum
AP,	Ansa peduncularis	CN,	Corticonigral tract
BC,	Brachium conjunctivum	CP,	Corticopulvinar fibers
BIC,	Brachium of inferior colliculus	CR,	Conjunctival radiation

→

anterior nucleus go to the frontal cortex. (4) Fibers from the anterior nucleus pass to the cingulate cortex concerned with consciousness. The gyrus also sends fibers to the tegmental region.

Visceral receptive areas, according to Penfield and Rasmussen (1950), and Penfield and Jasper (1954), occupy a wide zone of cortex from the posterior orbital cortex to the insula and inferior frontal gyrus. Their contributions in this field are of foremost importance (1954). Other studies of this region may be cited (Fulton, Pribram, Stevenson 1949). It is notable that this visceral area is underlaid by the claustrum CLA and extends into the region of the amygdala. These visceral areas are supplied by fibers from the above mentioned thalamic nuclei. The fibers probably carry visceral impulses. The interconnections in these regions appear appropriate for visceral functions and reactions (MacLean 1950). The anterior temporal nucleus (fig. 1, ATE) is a bridge of cortex between the uncinate cortex and temporal polar area 38. Farther back a similar bridge joins the hippocampal gyrus.

Reticular nucleus R is a shell of nerve cells that surrounds the dorsal thalamus on its lateral and anterior sides (fig. 1-7). It is a derivative of the ventral thalamus and is functionally related to the intralaminar nuclei. All parts of the reticular nucleus receive fibers from the intralaminar nuclei, a condition grounded in phylogeny. Its cells send fibers into the internal capsule which presumably go to the occipital, temporal, parietal and frontal regions of the cortex. The number of cells in the reticular nucleus is small in comparison with the cortical cell population among which its sparse fibers terminate. To this extended cortex they conduct non-specific impulses coming from the reticular formation to the intralaminar and thence to the reticular nucleus and cortex. The cortical cellular mechanisms for production of alpha group of rhythms is not fully

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DT, Deep tegmental nucleus
EXT, External capsule
F, Fornix
FN, Frontonigral tract
FP, Frontopontile tract
FR, Frontal radiation
G, Granule cell nuclei
H, Habenular nuclei
HIP, Hippocampus
HYP, Hypophysis cerebri
I, Intralaminar bundle
INS, Insula
INT, Internal capsule
IP, Inferior thalamic peduncle
IS, Interstitial spinal tract
L, Nucleus limitans
LA, Lateral anterior nucleus
LD, Lateral dorsal nucleus
LG, Lateral geniculate nucleus
LOT, Lateral olfactory tract
LP, Lateral posterior nucleus
MAR, Marginal nucleus of BC
MB, Mamillary body
MD, Medial dorsal nucleus
MG, Medial geniculate nucleus
ML, Medial lemniscus
MLF, Medial longitudinal fasciculus
MR, Medial cingulate radiation
MT, Mamillothalamic tract
NB, Nucleus basalis
OC, Occipital visual radiation
OH, Olfacto-, CH, corticohabenular tracts
OLF, Olfactory bulb
OR, Orbital radiation
OT, Optic tract
P, Posterior commissure
P_1, P_2, Inner and outer pallidum
PA, Paraventricular nucleus
PB, Parabigeminal nucleus
PC, Paracentral nucleus
PED, Cerebral peduncle
PF, Parafascicular nucleus
PH, Pallidohypothalamic fibers
PR, Prerubral field
PRT, Tectopretectal tract
PT, Ventral pretectal nucleus
Pul, Pulvinar
Put, Putamen
R, Reticular nucleus of thalamus
RN, Red nucleus
RTT, Reticulothalamic tract
SF, Subfascicular nucleus
SG, Supragenicular nucleus
SM, Submedial nucleus
SN, Substantia nigra
SO, Supraoptic nucleus
ST, Spinothalamic tract
SU, Subthalamic nucleus
SX, Subthalamic decussation
TGT, Tegmentothalamic tract
TP, Tectopontile tract
TR, Temporal radiation
TS, Terminal stria
TT, Tectothalamic tract
TUB, Olfactory tubercle
UF, Uncinate fasciculus
VA, Ventral anterior nucleus
VG, Ventral geniculate nucleus
VH, Ventral hypothalamic nucleus
VL, Ventral lateral nucleus
VM, Ventral medial nucleus
VP, Ventral posterior nucleus
VPM, Ventral posterior medial nucleus
VR, Ventral thalamic radiation
VTT, Trigeminothalamic tract
ZI, Zona incerta

understood. Jasper 1949 showed in a diagram how the non-specific and specific afferents to the cortical pyramids and granule cells may cooperate to produce rhythms (fig. 8).

Ventral thalamus is the original part of the reticular nucleus. It is of ancient origin and has many old connections especially those to the hypothalamus and basal ganglia. Medially it has extensive connections with the hypothalamus, and laterally with the reticular nucleus. Posteriorly is the red nucleus and its prerubral connections. To its side is the subthalamic nucleus of Luys which receives the pallidosubthalamic fibers. It sends fibers to the prerubral nucleus of the other side and thus regulates rubral discharge. The crossing fibers form the subthalamic (supramamillary) decussation. On the lateral side are the small ventral parts of the medial and lateral geniculate bodies. In front of the red nucleus scattered cells are associated with pallidosubthalamic, prerubral and pallidothalamic tracts. Notable are prerubral nucleus, nucleus campi Foreli and zona incerta. They have distinctive connections. The nucleus filiformis is related to the ventral thalamic radiation in front of the zona incerta, and is rudimentary.

Zona incerta ZI is located in the front part of the ventral thalamus. It has two afferent connections, large in rabbit, sheep and horse but small in primates. The geniculoincertal tract comes from the ventral part of the lateral geniculate, an optic reflex nucleus. The tegmentoincertal tract comes from the midbrain tegmentum with the median longitudinal fasciculus and is derived from vestibular sources. It passes over the red nucleus, ends in the zona incerta and forms a small dorsal supraoptic decussation. Some of its fibers pass out to the basal ganglia and temporal cortex. There is also a rudimentary pregeniculate (optic) nucleus which sends some vague fibers through the anterior perforated substance to the septum pellucidum.

Ventral thalamic radiation VR comes from the region of the zona incerta in the ventral thalamus. In primates it is a strong tract of fibers going to the pallida (Papez 1940). It is a V-shaped bundle of fine fibers applied to the edge of the internal capsule FR. Its position is lateral to the inferior thalamic peduncle IP and in front of the ansa peduncularis (lenticularis) with which it blends. Its fibers spread over the inner surface of the frontal radiation of the internal capsule, pass between its fibers and enter the pallida where its fibers disperse. The zona incerta with its ventral radiation to the pallida is probably an automatic orientating mechanism, fairly well developed in man. In general, the ventral thalamus through its afferent, and efferent motor connections serves to regulate automatically activities of the pallida, subthalamic and red nuclei and the adjacent hypothalamus. A basic physiologic mechanism of granule cells in the caudate nucleus and putamen may be concerned (Papez 1955). There is evidence that inhibition is associated with granule cells in various parts of the nervous system where large conduction neurons and axons occur (Papez 1955).

Mechanisms of cortical rhythms (fig. 8). A mechanism of non-specific EEG rhythms appears to be present in the outer layers of the cortex. This was represented in a diagram by Jasper (1949). Figure 8 shows non-specific axons 1 from the reticular nucleus of the thalamus R ending on pyramidal cells P in the upper part of layer three. When stimulated, the pyramidal cells fire down along their axons A to the thalamus. Their apical dendrites DA *backfire* into layer one where they spread to make contacts with dendrites coming from granule cells of layer two. These granule cells discharge their axons into nets which they form around pyramidal cells in layer three. Stimulation applied to surface of cortex produces functional arrest (Penfield and Rasmussen 1950; Kaada 1951; Penfield and Jasper 1954). Stimulation of granule cell aggregates elsewhere is associated with inhibition (Papez 1955). The facts suggest that the arrangement for backfire of apical dendrites into dendrites of granule cells in the outer layers of cortex may be the actual substance that produces consciousness. If this is so it would be an episensory function for layer three and an epimotor function for layer five.

The origin of neuropil in the superficial layers of the brain of amphibia has been often discussed by C. J. Herrick (1924-1927).

Present interest in these layers is a tribute to this distinguished author, C. J. Herrick.

Evolution of intralaminar and reticular nuclei is seen in a transitional stage in brains of reptiles (Papez 1935). There the intralaminar nuclei called reuniens are fused across the midline forming a massa intermedia. The reuniens nucleus surrounds the round medial dorsal nucleus on its ventral and lateral sides as in mammals. From the reticular formation a bulbothalamic tract comes up to end in the reuniens nucleus. From the tectum of the midbrain a tectothalamic tract ends in the same way on the lateral side. A tractus tectoreuniens comes across to the posterior end of the nucleus reuniens from the ventral medial geniculate nucleus and brings in vibrations. We may assume that the nucleus reuniens breaks up into the intralaminar groups in mammals. In the reptiles the nucleus reuniens sends fibers into the ventral thalamus and reticular nucleus which together form a common structure. Only the reuniens, medial and anterior nuclei are developed in the reptiles. They send a large dorsal peduncle into the corpus striatum. The posterior and lateral thalamic nuclei are lacking in reptiles. Their position is occupied by an extensive ventral thalamus and reticular nucleus. There is an absence of dorsal parts of lateral geniculate, medial geniculate, ventral posterior, ventral lateral, lateral dorsal, lateral posterior and pulvinar. No fully developed lemniscal systems enter this region in the reptiles. The ventral thalamus and reticular nucleus in reptiles lie directly beneath and to the side of the reuniens (intralaminar) which sends fibers into them. When the posterior and lateral nuclei grow into this region they separate the nucleus reuniens from the ventral thalamus and reticular nucleus, and a mammalian condition results. The condition in the reptiles can be reproduced in the dog by removing the entire neocortex which causes a degeneration of the posterior and lateral nuclei and reveals the fiber connections between the intralaminar and reticular nuclei (Papez and Rundles 1936). The rudimentary forebrain of reptiles has differentiated nerve cells in layer two which are reached by olfactory and reticular afferents. A deep ependymal layer is in the undifferentiated state.

SUMMARY

Intralaminar nuclei include parafascicular, limitans, centrum medianum, central, paracentral and central lateral, all situated along the length of the internal medullary lamina of the dorsal thalamus. The reticular thalamic, tegmentothalamic and tectothalamic tracts end in these nuclei which give rise to fibers that go out to end in the reticular nucleus on the outer surface of the thalamus. The reticular nucleus sends non-specific fibers to all parts of the cerebral cortex. The parafascicular and nucleus limitans send fibers to the reticular nucleus from which fibers go to the occipital cortex. Centrum medianum, near its middle, sends fibers ventrally and out to the ventral part of the reticular nucleus. An intralaminar bundle of fibers comes out of the frontal end of centrum medianum and ends in the central, paracentral, central lateral and submedial nuclei. Large cells in the bundle send fibers ventrally and out to the lower part of the reticular nucleus. Central and paracentral nuclei send fibers in the internal medullary lamina to the central lateral nucleus. From this nucleus fibers pass over the lateral anterior nucleus to reach the dorsal margin of the reticular nucleus. Central, paracentral and submedial nuclei send fibers in the inferior thalamic peduncle to the anterior perforated substance, and also fibers forward to the reticular nucleus and frontal cortex. Some fibers cross in the massa intermedia. Ventral medial and ventral anterior nuclei send fibers into the frontal radiation to the reticular nucleus and visceral areas in the medial frontal, orbital, insular and inferior frontal cortex. Ventral thalamus sends fibers to the hypothalamus, pallida and prerubral nucleus.

Reticular nucleus is the last link in the non-specific path to the cortex for EEG rhythms related to general consciousness. The non-specific neural system is distinct from specific sensory and other neural systems that activate the cortex. In the cortex the non-specific fibers from the reticular nucleus contact pyramidal and granule cells whose

actions produce the non-specific E E G rhythms.

REFERENCES

AJMONE-MARSAN, C. and DILWORTH, M. Non-specific projection system of the thalamus and striate system. Electrophysiological study. III Internat. Congress of EEG Neurophysiol., Boston, **1953**, Aug. 16-21.

BAILEY, PERCIVAL. Presidential address. Chicago, June 14, 1955. Symposium on electrical activity of subcortical centers. *Trans. Amer. Neurol. Assoc.*, **1955**.

DROOGLEEVER-FORTUYN, J. and STEFENS, R. On the anatomical relations of the intralaminar and midline cells of the thalamus. *EEG Clin. Neurophysiol.*, **1951**, *3*: 393-400.

FLECHSIG, P. Die Leitungsbahnen im Gehirn und Rukenmark des Menschen auf Grund entwicklengsgeschichtlicher Untersuchungen. Leipsig, W. Engelmann, **1876**, 382 pp.

FULTON, J. F., PRIBRAM, K. H. and STEVENSON, J. A. F. Interrelations between orbital gyrus, insula, temporal tip and anterior cingulate. *Program Amer. Neurol. Assoc.*, **1949**, 37-38.

HANBERY, J., AJMONE-MARSAN, C. and DILWORTH, M. Pathways of non-specific thalamo-cortical projection system. *EEG Clin. Neurophysiol.*, **1954**, *6*: 103-118.

HANBERY, J. and JASPER, H. Independence of diffuse thalamo-cortical projection system shown by specific nuclear destruction. *J. Neurophysiol.*, **1953**, *16*: 252-271.

HERRICK, C. J. Amphibian forebrain. *J. Comp. Neur.*, **1924-1927**, vols. 37, 39, 43.

HESS, W. R. and MÜLLER, H. R. Einflusse des Mittle- und Zwischenhirns auf die Atmung. *Helv. Physiol. Acta*, **1934**, *4*: 347-358.

JASPER, H. Diffuse projection system: the integrative action of the thalamic reticular system. *EEG Clin. Neurophysiol.*, **1949**, *1*: 405-419.

JASPER, H. and AJMONE-MARSAN, C. Thalamo-cortical integrative mechanisms. *Res. Publ. Ass. nerv. ment. Dis.*, **1950**, *30*: 493-512.

JOHNSON, F. H. Neuro-anatomical tracts considered as correlates of ascending reticular activating system in the cat. *Anat. Rec.*, **1953**, *115*: 327-328.

KAADA, B. R. Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of rhinencephalic and other structures in primates, cat and dog. *Acta Physiol. Scand.*, **1951**, vol. 23, Suppl. 83. (Much information on inhibition is contained in this volume).

KUHLENBECK, H. *The human diencephalon.* New York, S. Karger, **1954**, pp. 230.

LEVINE, P. M. *The precentral cortex.* P. C. Bucy editor. Urbana Ill., Univ. Ill. Press, **1944**, ref. p. 143.

MACLEAN, P. D. Psychosomatic disease and the "visceral brain"; recent developments bearing on Papez theory of emotion. *Psychosom. Med.*, **1950**, *11*: 338-353.

MAGOUN, H. W. An ascending reticular activating system in the brain stem. *Arch. Neurol. Psychiat.*, Chicago, **1952**, *67*: 145-154.

MORUZZI, G. and MAGOUN, H. W. Brain stem formation and activation of the EEG. *EEG Clin. Neurophysiol.*, **1949**, *1*: 455-473.

PAPEZ, J. W. and ARONSON, L. R. Thalamic nuclei of Pithecus rhesus. *Arch. Neurol. Psychiat.*, Chicago, **1934**, *32*: 1-44.

PAPEZ, J. W. Thalamus of turtles and thalamic evolution. *J. Comp. Neurol.*, **1935**, *61*: 433-475.

PAPEZ, J. W. Evolution of the medial geniculate body. *J. Comp. Neurol.*, **1936**, *64*: 41-61.

PAPEZ, J. W. and RUNDLES, R. W. Thalamus of dog without a hemisphere due to unilateral congenital hydrocephalus. *J. Comp. Neurol.*, **1938**, *69*: 89-102.

PAPEZ, J. W. A. Summary of fiber connections of basal ganglia with each other and with other portions of the brain. *Res. Publ. Ass. nerv. ment. Dis.*, **1940**, *21*: 21-68.

PAPEZ, J. W. and STOTLER, W. A. Connections of the red nucleus. *Arch. Neurol. Psychiat.*, Chicago, **1940**, *44*: 776-791.

PAPEZ, J. W. Granule cells, their distribution in the central nervous system, considered as an inhibitor system. *Anat. Rec.*, **1955**, *121*: 411.

PENFIELD, W. and RASMUSSEN, T. *The cerebral cortex of man. A clinical study of localization of function.* New York Macmillan, **1950**, pp. 248.

PENFIELD, W. and JASPER, H. *Epilepsy and the functional anatomy of the human brain.* Boston, Little, Brown and Co., **1954**, pp. 896.

PITTS, R. F. Organization of the respiratory center. *Physiol. Rev.*, **1946**, *26*: 609-630.

RUNDLES, R. W. and PAPEZ, J. W. Connections between the striatum and the substantia nigra in a human brain. *Arch. Neurol. Psychiat.*, **1937**, *38*: 550-563, ref. p. 559.

RUSSELL, G. V. The dorsal trigemino-thalamic tract in the cat reconsidered as a lateral reticulothalamic system of connections. *J. Comp. Neurol.*, **1954**, *101*: 237-263.

SINGER, M. and YAKOVLEV, P. I. *The human brain in sagittal section.* Springfield Ill. C. C. Thomas, **1954**, pp. 81.

STARZL, T. E. and MAGOUN, H. W. Organization of the diffuse thalamic projection system. *J. Neurophysiol.*, **1951**, *14*: 133-146.

UNESCO and WHO. *Brain mechanisms and consciousness.* A symposium organized by the council for international organization of medical sciences. Springfield Ill. C. C. Thomas, **1954**.

WALKER, A. E. *The primate thalamus.* Univ. of Chicago Press, **1938**, pp. 321.

WALKER, A. E. Discussion of paper of Yakovlev. *Trans. Amer. Neurol. Assoc.*, **1954**, p. 53.

WALKER, A. E. Meaning of thalamus. Unspecified thalamic system. VI Congreso Latinoamericano de Neurocirugía. Montevideo, **1955**, p. 306.

WEINSTEIN, W. A. and BENDER, M. B. A motor pattern of emotional expression elicited on brain stem stimulation. *Program Amer. Neurol. Assoc.*, **1947**, p. 63.

YAKOVLEV, P. I. Anatomical studies in frontal leucotomies. *Trans. Amer. Neurol. Assoc.*, **1954**, 53-56.

Reference: PAPEZ, JAMES W. Central reticular path to intralaminar and reticular nuclei of thalamus for activating EEG related to consciousness. *EEG Clin. Neurophysiol.*, **1956**, *8*: 117-128.

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SIMULTANEOUS EEG-EKG RECORDING : STUDY OF A CASE WITH COMPLETE HEART BLOCK AND PAROXYSMAL VENTRICULAR TACHYCARDIA

JOLYON S. TUCKER, M.D. and ROBERT H. YOE, M.D.
Division of Neurology and Department of Medicine, Medical College of Alabama, Birmingham, Ala.

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Adams-Stokes seizures in a patient with complete heart block and paroxysmal ventricular tachycardia afforded an unusual opportunity to make simultaneous electroencephalogram-electrocardiogram (EEG-EKG) recordings in this condition. Another case presenting EKG evidence of myocardial irritability but having seizures unrelated to cardiac arrythmia is reported to demonstrate the usefulness of such simultaneous recordings.

Fig. 1

Simultaneous EEG-EKG tracing between attacks in case I. EEG shows slight excess of fast activity but is otherwise normal. EKG shows complete A-V block with idioventricular rhythm and premature ventricular beats. Odd number left side and even numbers right side. Fp — frontopolar, C — central, T — temporal, O — occipital, A — auricular, EKG — arm to arm (lead I).

CASE REPORTS

CASE I: Mrs. C. M., age 58, was admitted to the neurology service, University Hospital, Medical College of Alabama, on November 1, 1954, because of frequent episodes of unconsciousness and sometimes convulsions. A typical episode was preceded by a "rising feeling" and then a pounding in the chest. She was then said to become pale around the mouth and to complain of being hot. Following this she became unconscious and sometimes had a tonic convulsion with incontinence. A previous diagnosis of rheumatic heart disease had been made and she had been treated for congestive heart failure in June 1954, but had received no digitalis for two months. She had experienced attacks for three months, but for several days preceding admission had been having seizures every 30 to 40 min. Physical examination revealed a middle-aged white female having frequent seizures and who gave the appearance of being chronically ill. The seizures were either short episodes of staring and unconsciousness or consisted of tonic extension of the trunk and neck without clonic movements. Blood pressure was 170/65, pulse 38 and ir-

regular, respirations 20. There were loud systolic and diastolic murmurs over the precordium. During attacks the apical rate was recorded as 160 and regular. The heart appeared to be enlarged to the left. There was venous distension, hepatomegaly and pedal edema. Neurological examination was normal.

The patient was treated with oxygen, lanatoside C, Thiomerin, quinidine gluconacte, and potassium chloride. Longer and longer runs of ventricular tachycardia occurred. She finally became comatose and expired 60 hours after admission.

A simultaneous EEG-EKG was made (fig. 1 and 2). On this tracing the resting EEG showed a slight excess of fast activity but was otherwise normal. The EKG showed complete atrio-ventricular block and premature ventricular beats. Bouts of paroxysmal ventricular tachycardia were recorded and when they persisted for over 10 sec. the brain rhythms slowed considerably and a short period of confusion, pallor, tachypnea and staring occurred. Short tonic convulsions occurred after runs of tachycardia lasting 18 sec. or longer. After long runs of tachycardia the EEG assumed ''flat'' characteristics (fig. 3).

Autopsy showed signs of old rheumatic heart disease with multiple valvular lesions as well as extensive areas of fibrosis throughout the myocardium. There was also evidence of myocardial failure. Gross examination of the brain showed no abnormality; microscopic examination revealed mild diffuse cortical nerve cell changes consistent with anoxia.

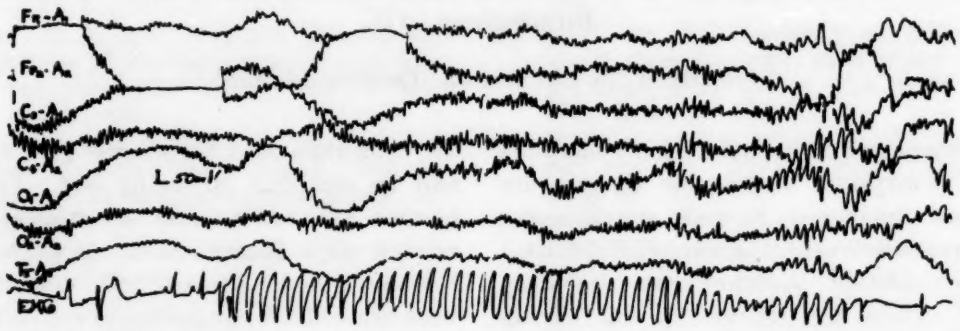

Fig. 2

Case I, EKG demonstrates extreme myocardial irritability with premature ventricular beats leading into a 13 second run of paroxysmal ventricular tachycardia with a rate of 210. After 10 sec. of tachycardia there is a perceptable slowing in the EEG with the appearance of high voltage theta activity preceding a short episode of confusion, staring, pallor and tachypnea.

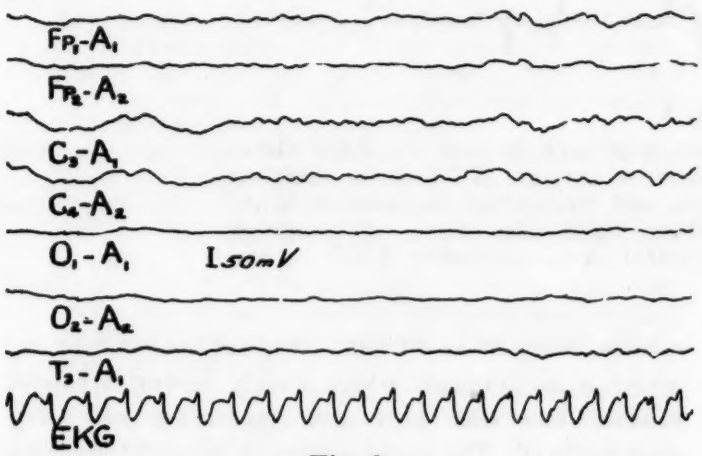

Fig. 3

Case I, recording after 3 min. of continuous ventricular tachycardia. EEG assumes ''flat'' characteristics.

CASE II: Mrs. A. M., age 77 was admitted to the medical service because of frequent convulsions thought to be due to cardiac disease. She gave a history of having had almost continual convulsions for 4 days. The convulsions had consisted of extension of the body with flexion of arms, and had become increasingly frequent after she developed a fever of 104 degrees F. Forty five years prior to admission the patient had had ''inflammatory rheumatism and inflammation of the heart''. Since that time she had been having infrequent seizures which had consisted mostly of collapsing as if in a faint. She had been taking diphenylhydantoin, 0.2 gm. daily, with fairly good control of these episodes. For many years she had rheumatoid arthritis and spondylitis for which she had recently been given cortisone. Her physician had noted some cardiac irregularity and had referred her for further investigation.

On examination the patient seemed confused and was having frequent convulsions. Some of these consisted of a tonic extension with upward movement of the eyes but no clonic movements. In other seizures there was tonic extension of the right arm with rotation of the head to the right and upwards. The sei-

zures lasted about 15 to 20 sec. each. Blood pressure was 140/78, pulse 100 and irregular. There were rheumatoid deformities of all extremities. The heart appeared to be of normal size. There was a loud apical systolic murmur. There was moderately severe retinal arteriosclerosis. Neurologic examination revealed a snout reflex, bilateral tongue weakness, and slurred speech. The Babinski and Gordon signs were positive on the right. The remainder of the examination was essentially negative.

A simultaneous EEG-EKG was made (fig. 4 and 5). This revealed frequent auricular and ventricular premature beats, but the cardiac rhythm was regular during several clinical seizures which were observed and at the same time the cerebral rhythms showed a high voltage rhythmical 4/sec. activity which was mostly localized in the left fronto-central region. This was not due to movement artifact. The patient was treated with intramuscular sodium phenobarbital, diphenylhydantoin, trimethadione and primidone and the seizures were quickly brought under control. Later the patient was treated for heart failure. She was discharged on the seventh hospital day, free from seizures and with normal cardiac rhythm.

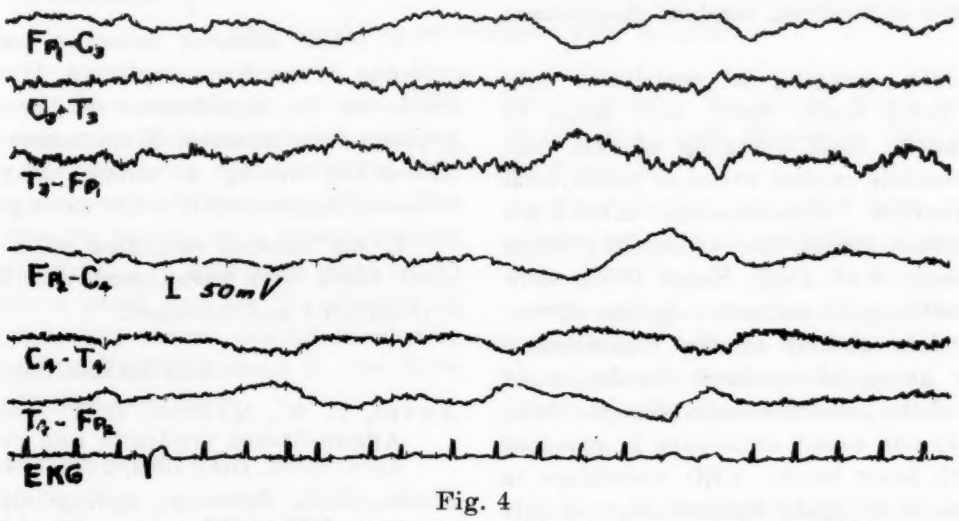

Fig. 4

Case II, resting EEG shows mostly low voltage fast activity. EKG shows myocardial irritability with frequent auricular and ventricular premature beats.

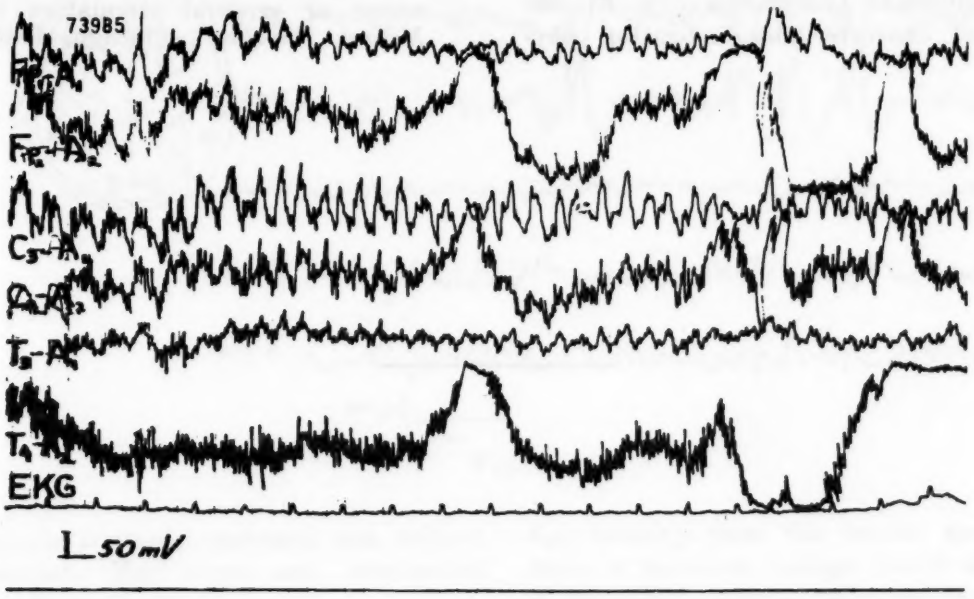

Fig. 5

Case II, tracing performed during a seizure in which the patient extended the right arm and had tonic extension of the head and neck. EKG shows regular rhythm. EEG shows high voltage 4/sec. paroxysmal activity principally in the left frontal and central regions.

DISCUSSION

Despite evidence of heart disease in both patients the simultaneous records clearly indicated that the convulsions were secondary to cardiac arrythmia in case I and secondary to localized cerebral disturbance in case II.

It is the sudden changing of ventricular rate rather than the heart block, itself, that leads to Adams-Stokes seizures. Such changing of rate may consist either of complete cardiac arrest or paroxysmal ventricular tachycardia. Simultaneous EEG-EKG recordings in cardiac arrest due to carotid sinus stimulation (Roseman *et al.* 1945; Engel 1950) show generalized delta activity 10 sec. after cardiac arrest. This response is very similar to the experimental findings in acute arrest of cerebral circulation of man by occlusion of the carotid vessels (Rossen 1943) and would be what one would anticipate in cases of cardiac arrest with heart block. EEG recordings in such a case (Amyes *et al.* 1953) however, showed only diminution in the amplitude of the electrical activity and slight slowing, but no simultaneous record of the EKG was available in this case. In case I the degree of slowing is less than that produced in the cases due to carotid sinus stimulation. This would be in keeping with the fact that in paroxysmal ventricular tachycardia the cardiac output is greatly reduced but not completely arrested. Nevertheless, after sustained ventricular tachycardia (fig. 3), the EEG assumed flat characteristics indicating physiological decortication (Fois 1955). At this time the patient no longer had seizures although the tachycardia persisted.

SUMMARY

1. When seizures occur in patients who show evidence of cardiac arrythmia, it is often hard to decide on the significance of the arrythmia in the genesis of the seizures. Simultaneous recording of the EEG-EKG during a seizure may supply critical evidence as illustrated in the cases presented.

2. An unusual recording in a case of complete heart block with paroxysmal ventricular tachycardia is illustrated and discussed.

REFERENCES

AMYES, E. W., MAHONY, D. V. and GOODMAN, R. D. Adams-Stokes syndrome and cerebral anoxia. *J. nerv. ment. Dis.*, **1953**, *117*: 334-340.

ENGEL, G. L. *Fainting.* Springfield, Charles C. Thomas, **1950**, p. 39.

FOIS, A., GIBBS, E. L. and GIBBS, F. A. "Flat" electroencephalograms in physiological decortication and hemispherectomy. *EEG Clin. Neurophysiol.*, **1955**, *7*: 130-134.

ROSEMAN, E., WHITCOMB, B. B. and WOODSON, F. G. Carotid sinus syncope secondary to ligation of carotid vessels for intracranial arteriovenous aneurism. *J. Neurosurg.*, **1945**, *2*: 287-305.

ROSSEN, R., KABAT, H. and ANDERSON, J. P. Acute arrest of cerebral circulation in man. *Arch. Neurol. Phychiat.*, Chicago, **1943**, *50*: 510-528.

Reference: TUCKER, JOLYON S. and YOE, ROBERT H. Simultaneous EEG-EKG recording: Study of a case with complete heart block and paroxysmal ventricular tachycardia. *EEG Clin. Neurophysiol.*, **1956**, *8*: 129-132.

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FOCAL SPIKE AND WAVE ACTIVITY IN A PATIENT WITH HEADACHES

DEWEY K. ZIEGLER, M.D. and FERNANDO TORRES, M.D.
Division of Neurology, Montefiore Hospital, New York

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Focal spike and wave activity is a rare EEG pattern. Its occurrence in the absence of epilepsy is still more uncommon, occurring for example in only 3 cases out of a large series by Silverman (1954). The following case is thought worthy of a report because it is a rarity in two ways: (1) spike and wave activity was present over a small area, in the absence of seizures of any type; (2) severe orbital headaches precipitated by light and contralateral to the EEG focus were the presenting symptoms.

CASE REPORT

The patient is a 6½ year old female child, who is reported to have been in excellent health up to the age of 2½ years when she had a fairly severe and prolonged bout of whooping-cough. Since that time she has been subject to infrequent but fairly severe generalized headaches. Also since that time she has been excessively irritable, stubborn and subject to temper tantrums. Her motor and intellectual development have been normal.

Six months prior to the first EEG, after watching a motion picture for about an hour, she had an extremely severe pain centred about and behind the left eye. The pain disappeared after an hour but "itching and drawing" feelings persisted for a few hours in the same area. A similar episode occurred a few months later, not precipitated by a motion picture or other known source of light. Aside from these two episodes, the patient has been subject to her "regular" headaches, which are generalized but do not occur more frequently than once every two or three months.

The mother and child both deny any type of seizure, syncope, or distortion of consciousness at any time.

Neurologic examination, including plotting of visual fields, reveals no abnormalities. The child is alert and of normal intelligence. She is, however, as noted, unstable, stubborn, and subject to temper tantrums.

ELECTROENCEPHALOGRAMS

All records were taken on a Grass 8-channel model III machine.

The record on March 25, 1955 showed a mixture of 4-7 c/sec. activity from all leads and low voltage fast activity from the frontal areas. There was a focus of moderate voltage (50-75 mV.) delta activity in the right posterior temporal-lateral occipital area, with infrequent low voltage spikes. Hyperventilation for 2 min. caused gradual appearance of bilateral generalized high voltage 2-4 c/sec. activity, but no spikes, no clinical phenomena and no accentuation of the focal pattern. The record was repeated three times at monthly intervals. On each of the succeeding records the general pattern was within normal limits for the age. The small focus of electrical abnormality in the posterior temporal-lateral occipital area persist-

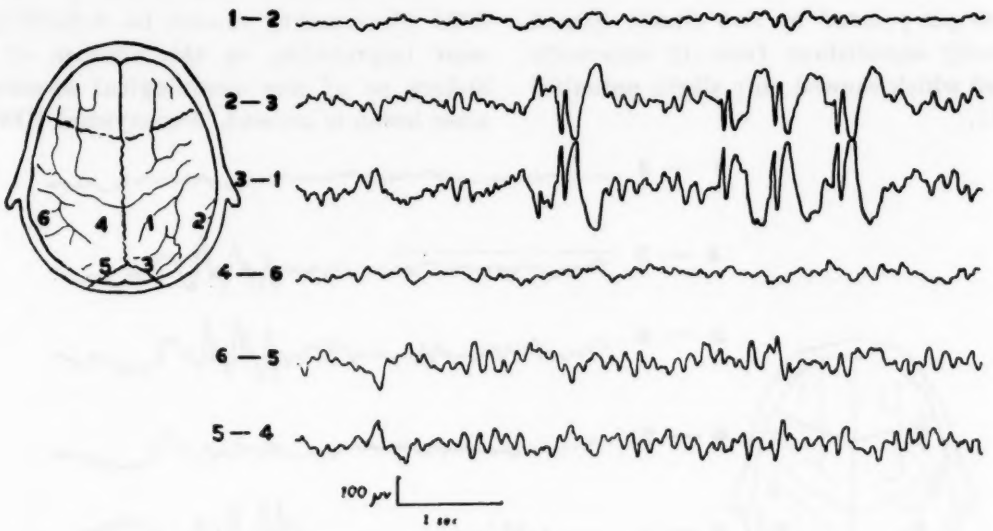

Fig. 1

ed, but in these later records the abnormal activity consisted of numerous high voltage, brief paroxysmal bursts of spike and wave complexes (fig. 1). The form of the complex varied markedly with relation of the complex was most prominent, it seemed definite that near the focus the bursts consisted of one or more complexes of spike and dome, the frequency varying from 2-4 c/sec.

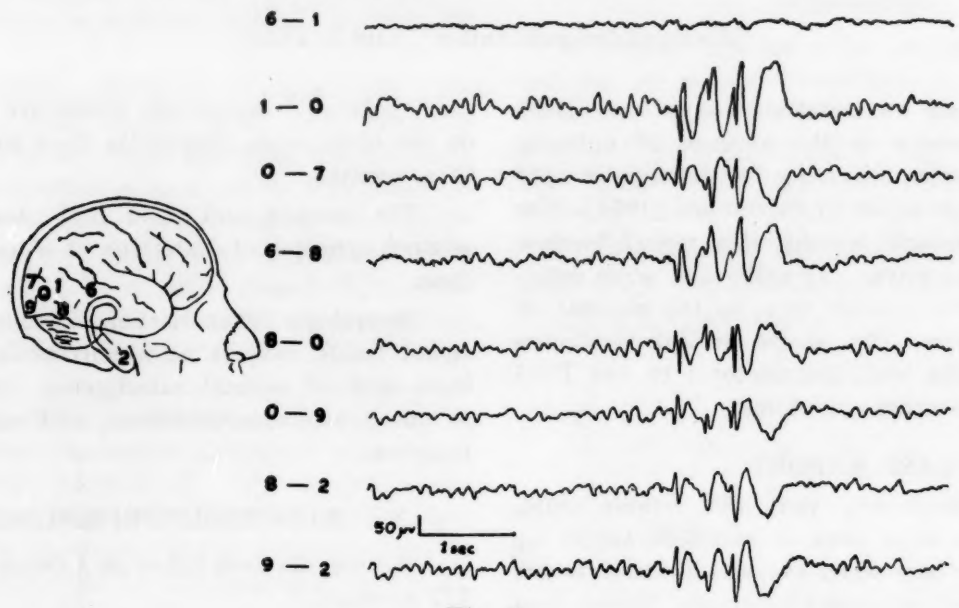

Fig. 2

of the recording electrode to the centre of the focus (fig. 2).

The focus was pin-pointed by two closely placed electrodes apparently equidistant from it anteriorly and posteriorly and which showed only slight potential difference (fig. 3).

COMMENT

The nature of the lesion producing this focal EEG abnormality cannot be definitely stated. It is most improbable, in the absence of a progressive history or of any neurological abnormalities that a mass lesion is present. Paroxysmal EEG abnormalities

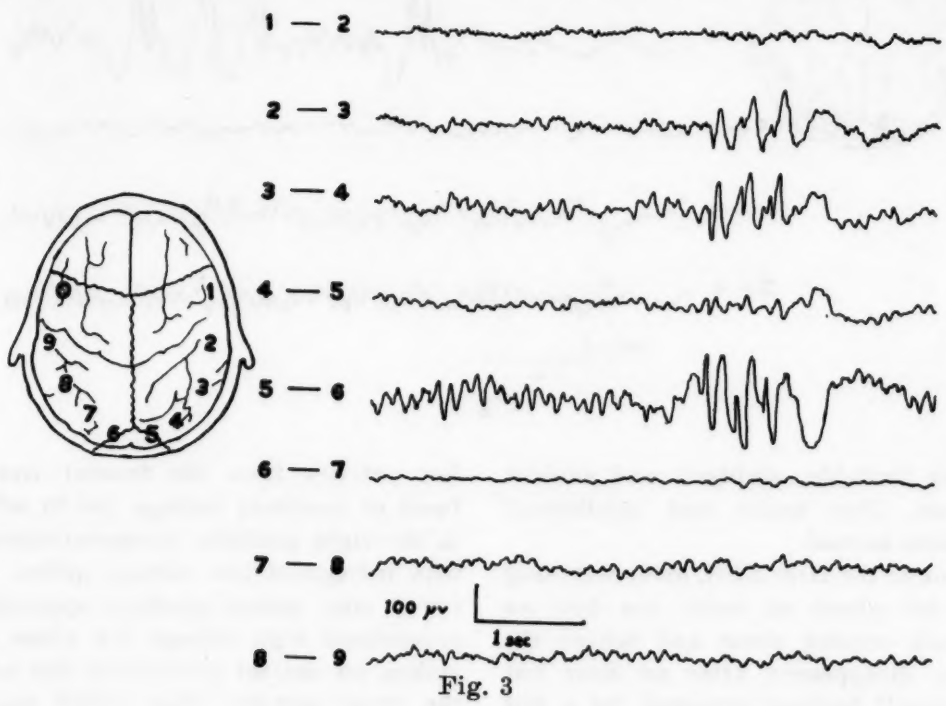

Fig. 3

The paroxysmal activity was not accompanied by an electrical disturbance elsewhere in the hemisphere or on the opposite side (fig. 3). Although at times the spike and at other times the slow wave component are, furthermore, uncommon with the latter. It is more probable, with the history of headache and behavior disturbance since whooping cough, that an area of cerebral tissue was damaged either by in-

farction or an encephalitic process during that illness, and is responsible for the EEG focus. Recent reports have indicated that severe EEG abnormalities may accompany virus infections of childhood (Dreyfus-Brisac *et al.* 1954; Grossman *et al.* 1955).

It seems quite possible that the two severe left orbital headaches, one of which was precipitated by light, were focal epileptic "equivalent" phenomena. Focal spike and wave in the EEG in the absence of epilepsy has been reported as an extremely rare occurrence. On the other hand, some patients with migraine, particularly when they present clinical evidence of involvement of the nervous system, have paroxysmal records (Weil 1952; Dow and Whitty 1947). Similarly, paroxysmal electrical abnormalities are found in patients with episodic visceral pain, e.g., abdominal pain, and these painful crises are now well recognized as related to cerebral dysrhythmia (Hoefer *et al.* 1950; Moore 1945).

REFERENCES

Dow, D. J. and Whitty, C. W. M. Electroencephalographic changes in migraine: Review of 51 cases. *Lancet*, **1947**, *2*: 41-78.

Dreyfus-Brisac, C., Beanben, E. and Mises, R. EEG changes in 13 cases of non-complicated whooping cough in children. *EEG Clin. Neurophysiol.*, **1954**, *6*: 526.

Grossman, H. J., Gibbs, E. L., Lepper, O. H. and Spies, H. W. Electroencephalographic studies in children with measles with no clinical evidence of central nervous system involvement. *EEG Clin. Neurophysiol.*, **1955**, *7*: 315.

Hoefer, P. F. A., Cohen, S. M. and Greeley, D. M. Paroxysmal abdominal pain, an epileptic equivalent. *Trans. Amer. Neurol. Assoc.*, **1950**, p. 183.

Moore, M. T. Paroxysmal abdominal pain. A form of focal symptomatic epilepsy. *J.A.M.A.* Dec. 29, **1945**, *129*: 1233.

Silverman, D. Clinical correlates of the spike-wave complex. *EEG Clin. Neurophysiol.*, **1954**, *6*: 663.

Weil, A. A. EEG findings in a certain type of psychosomatic headache: dysrhythmic migraine. *EEG Clin. Neurophysiol.*, **1952**, *4*: 181-186.

Reference: Ziegler, Dewey K. and Torres, Fernando. Focal spike and wave activity in a patient with headaches. *EEG Clin. Neurophysiol.*, **1956**, *8*: 133-135.

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TECHNICAL NOTES

Editor for Western Hemisphere and Far East, J. KNOTT, Iowa City, Iowa, U.S.A.
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A METHOD FOR ACCURATE PLACEMENT OF ELECTRODES IN THE HYPOTHALAMUS OF THE DOG[1]

DAVID M. HUME, M.D.[2] and WILLIAM F. GANONG, M.D.[3]
Laboratory for Surgical Research, Harvard Medical School, Boston, Massachusetts and the Naval Medical Research Institute, Bethesda, Md.

(Received for publication: August 15, 1955)

The first accurate stereotaxic instrument for the production of localized brain lesions was designed by R. H. Clarke, and was briefly described by Clarke and Horsley in 1906. In 1920 Clarke published a detailed account of the later modifications of his original instrument. In 1908 Horsley and Clarke described the original instrument in some detail in an article concerned with its use in a study of cerebellar function. Subsequent modifications of this geneotype have become incorrectly known as Horsley-Clarke stereotaxic instruments, although it seems clear that Clarke alone was responsible for the development of the original machine (Horsley and Clarke 1908; Clarke and Henderson 1911; Clarke 1920; Mussen 1923; Sacks and Fincher 1927; Bailey and Stein 1951; Carpenter and Whittier 1952).

Many different models of stereotaxic instruments have been devised, and their use has been described for the cat and monkey (Horsley and Clarke 1908; Clarke 1920; Ranson 1934), the rat (Clarke 1939; Krieg 1946; Stellar and Krause 1954), the rabbit (Harris 1947; Sawyer *et al.* 1954), and the human (Spiegel *et al.* 1947; Jasper and Hunter 1949; Talairach *et al.*, 1949; Hayne and Meyers 1950; Bailey and Stein 1951; and others). Atlases are available for the monkey (Clarke and Henderson 1920; Mussen 1923; Atlas and Ingram 1937; Olszewski 1952), the cat (Clarke and Henderson 1911; Winkler and Potter 1914; Ingram *et al.* 1932; Gérard *et al.* 1936; Hess 1932; Jiménez-Castellanos 1949), the rat (Krieg 1946), the rabbit (Winkler and Potter 1911; Sawyer *et al.* 1954), and the human (Spiegel and Wycis 1952). A recent review of stereotaxic methods has been published by Carpenter and Whittier, 1952.

To increase the accuracy of localization of electrodes in the human, air ventriculograms (Talairach *et al.* 1949, 1950) and X-ray demonstration of intracranial calcification and encephalograms (Spiegel and Wycis 1952) have been carried out at a time previous to the actual placement of electrodes. More recently, ventriculograms have been obtained at the time the electrodes are placed, by introducing air into the lateral ventricles (Hodes *et al.* 1954). Hayne and Meyers (1950) performed pneumoencephalography in patients after the electrodes were in place. They apparently did not use air studies as an aid in the placement of the electrodes.

Localization by stereotaxic coordinates based on skull planes is unsatisfactory in the mongrel dog, as in the human, because of the great variability in the shape and size of the skull, and of the relation of the bony landmarks to the brain.

In the course of studies conducted over the past seven years, a method for accurate placement of electrodes in the hypothalamus of the dog has been perfected, and used both for stimulation and destruction of localized areas. In this method, localization is achieved by means of X-ray visualization of the third ventricle at the time the electrodes are inserted.

X-ray studies of the intact head and the sagittally split skull and brain were carried out in an effort to see if a constant relationship could be established between bony landmarks at the base of the skull and structures in the hypothalamus (Cowie and Hume). In another series of studies, needles were put down in various areas of the hypothalamus and fixed in place. The skull was X-rayed and the relationship of the needles to bony landmarks was noted. The animals were then sacrificed and the brain was immediately fixed by perfusion through the carotid arteries with saline followed by 10 per cent neutral formalin. Openings were made through the skull, and the brain and skull with the needles in place were fixed in formalin for an additional two weeks. At the end of this time the brain was cut, and serial sections of the hypothalamus were made to verify the actual location of the needles. A fairly good correlation between bony landmarks and the median eminence

[1] This work has been supported in part by a grant-in-aid from the Commonwealth Fund.

[2] Scholar in cancer research, American Cancer Society.

[3] Fellow of the National Institute of Neurological Diseases and Blindness.

was obtained, but the relationships were not accurate for other areas of the hypothalamus.

In the meantime, in the course of other studies on injection of substances into the third ventricle of the dog (Ganong and Hume) it was noted that radio-opaque compounds placed in the ventricle gave an excellent X-ray outline of the structures which bordered it. Furthermore, performing the ventriculogram was technically easy, and control experiments showed that it apparently did not harm the dog.

Performing a ventriculogram permits an excellent localization of those areas of the hypothalamus

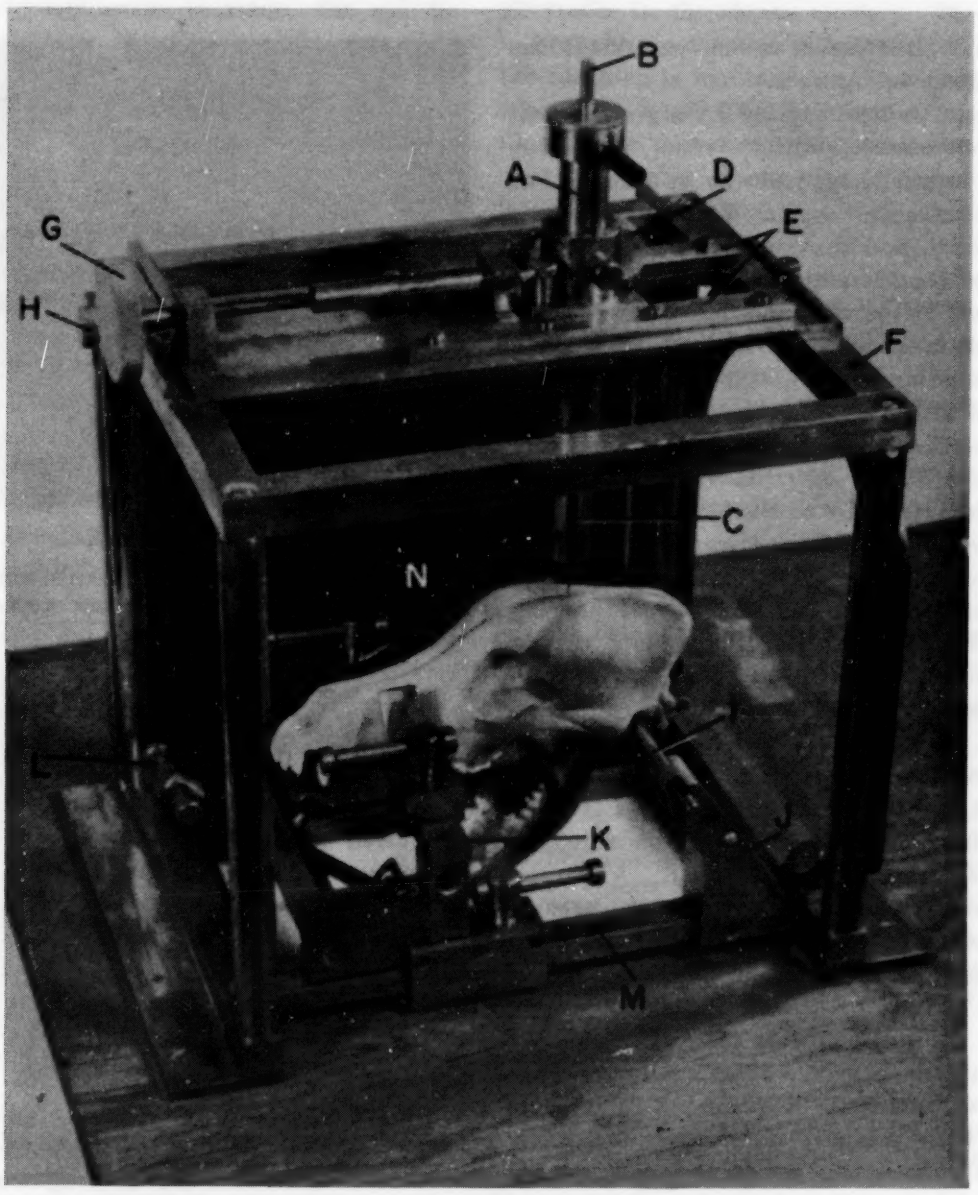

Fig. 1
The stereotaxic instrument.

A — spindle carrier
B — spindle (attaches to flexible cable from electric motor)
C — collet attached to spindle (removable for sterilizing)
D — brake which holds spindle carrier at any desired position
E — ways for motion of spindle carrier in sagittal plane
F — ways for motion of spindle carrier in frontal plane
G — wheel for adjusting sagittal motion
H — wheel for adjusting motion in frontal plane
I — ear plugs
J — ear plug holders
K — bar to hold upper jaw, with adjustable clamps
L — adjustable holder for lower jaw
M — ways for motion of jaw holder in A-P direction
N — X-ray casette in place in casette holder

which border the third ventricle. Two machines have been devised which make it possible to obtain accurate X-rays, and which can be used to implant stimulation needles or to make electrolytic lesions in the hypothalamus. Since all of the experiments are of a chronic nature, the machines have been designed to allow the use of aseptic technique with a minimum of difficulty.

The stereotaxic instrument which we use at the present time is shown in figure 1.[1]

The dog's head is held rigidly by stainless steel plugs which fit into each auditory canal, by a bar which holds the upper jaw, and by a second bar which holds the lower jaw open. The lower jaw is held open in order to pull the coronoid process of the mandible down so that it will not interfere with the clarity of the X-ray in the region of the hypothalamus. The horizontal plane of the skull is made parallel to that of the machine by means of the ear plugs.

The top shelf of the machine is supported by four posts which are attached to it, and the whole top framework can be lifted off the bottom at will, permitting complete exposure of the head. The spindle to which the collet is attached is driven by a variable speed electric motor whose power is transmitted to it through a flexible cable. A ball thrust bearing is incorporated into the top of the spindle carrier to reduce friction when drilling. The spindle carrier is adjustable in all directions, and is calibrated in all directions. A number of drills and electrode carriers have been machined to fit accurately in the collet. The collet, which is made of stainless steel, is removable and only the collet and the tools which fit into it need be autoclaved.

In use, the dog's head is clamped in the base of the instrument after the top framework has been removed. The head is shaved, prepped with iodine and alcohol, and draped with a sterile towel. A mid line incision 3.5 cm. in length is made through the scalp with the electro-cautery. The top framework of the machine is now put in place. A pointer is inserted into the collet and adjusted until it is directly over the sagittal suture. An X-ray casette is placed in the holder which is attached to the back of the machine in such a way that the casette is held at a fixed distance from the midline. A partial radio-opaque grid has been cut into the face of the casette to facilitate measurements. The X-ray tube is adjusted by levels and special guide bars so that the axis of the tube is perpendicular to the X-ray film and a constant distance from the film. It is further adjusted so that the center of the X-ray beam is at a point opposite to the spindle, and even with the floor of the third ventricle in a vertical plane. An ordinary portable X-ray machine can be used for this purpose. By using the center of the beam, distortion in the area of the film occupied by the hypothalamus is eliminated. The slight magnification which occurs is corrected by multiplying the measurements made in the film by a constant factor.

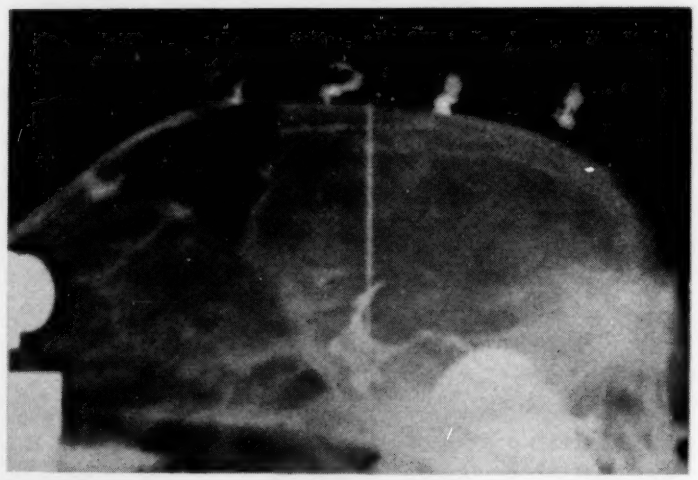

Fig. 2

X-ray demonstration of the third ventricle in the dog. A 0.1 cc. quantity of sodium acetrizoate has been injected into the ventricle.

An X-ray is now taken. The bony landmarks, while not strictly accurate, permit selection of a point which is roughly in the center of the third ventricle (± 1.5 mm.). The distance which the collet has to be moved to be above this point is ascertained by measurement directly from the film, and the collet is then moved until it is over the point. A 0.032 inch drill is placed in the collet and a hole is drilled through the skull in the midline, and above the center of the ventricle.

A 4 cm. hollow # 21 needle is inserted through the hole. The needle is allowed to project into the brain for a distance of about 2.5 cm. The ventriculogram is made with the use of a one foot long # 26 needle [2] attached to a one cc. syringe containing 70 per cent sodium acetrizoate [3]. An adjustable stop is placed on the 26 gauge needle so that it will penetrate the brain to a depth 1.3 cm. above the base of the skull, (as measured from the X-ray film). The # 26 needle is threaded through the # 21 needle, and is thus guided into the third ventricle. One-tenth of a cc. of Urokon is injected slowly and an X-ray is taken. A good outline of the third ventricle is thus obtained. (fig. 2). The supra-optic projection of the third ventricle, the outline of the optic chiasm, the

[1] This was designed by one of us (D. M. H.) in 1953, and was constructed by G. W. Pearse in the machine shop of the Naval Medical Research Institute, under the supervision of J. Bronson.

[2] The needles were manufactured for us by the MacGregor Instrument Company, Needham, Mass.

[3] Urokon Sodium®, Mallinckrodt Chemical Works, St. Louis, Mo.

entire median eminence, the infundibular projection of the ventricle, the posterior tuber, and the bulge made by the mammillary body, as well as the massa intermedia, the aqueduct and the anterior commissure are all outlined. This makes it possible to pick out very precisely the area which it is intended to stimulate or destroy.

After the ventriculogram is made, the spindle is brought to a position directly over the area into which it is desired to insert the electrode. A hole 6 mm. in diameter is drilled through the skull with the machine. An offset electrode carrier containing two # 21 needles is inserted into the collet. A projection from the bottom of the carrier goes down into the hole and rests on the dura, so that the needles will be given maximum support as they perforate the dura and extend part way through the brain. The electrodes are guided down through the needles, which support them to within one cm. of the end. For making lesions # 26 enamel coated copper wire is used. The insulation is scraped off the last 0.5 mm. of the tip. The tongue serves as the indifferent electrode.

Figure 3 is a drawing illustrating the "average" dimensions of the third ventricle and showing the

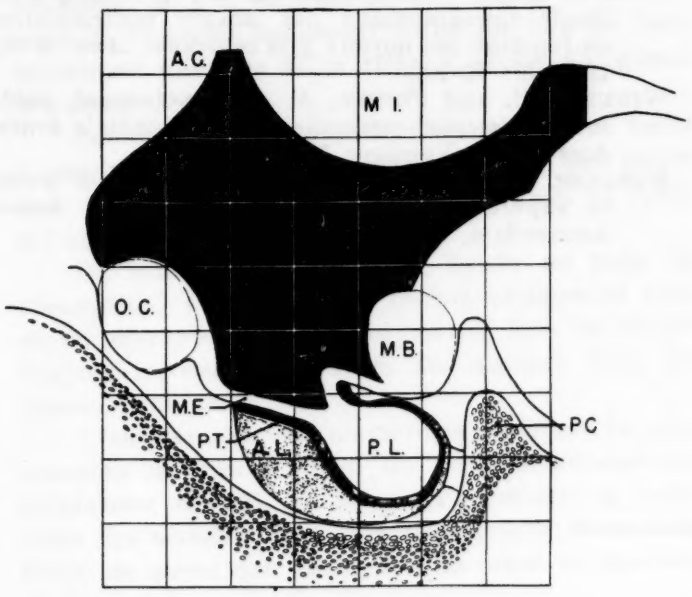

Fig. 3

"Average" dimensions for the third ventricle in the dog. The squares of the grid are 2 mm. on each side. The relationship of some of the structures of the hypothalamus and pituitary to the ventricle are shown. The solid black is the outline of the ventricle.

AC — anterior commissure
AL — anterior lobe of the pituitary
MB — mammillary body
ME — median eminence
MI — massa intermedia
OC — optic chiasm
PC — posterior clinoid
PL — posterior lobe of the pituitary
PT — pars tuberalis of the anterior pituitary

structures which can be identified on the ventriculogram. The average measurements taken from 50 ventriculograms were used to make this diagram. Considerable variation occurred from dog to dog, and for accurate placement of lesions a ventriculogram must be performed on each animal.

The instrument can also be used for placing electrodes in the rhesus monkey. The monkey's head is brought up through a hole in the board on which the machine is mounted, and ear plugs made for this species are used. The technique employed is otherwise identical to that described here for the dog.

An earlier instrument [1], also utilizing X-ray localization, employed an adjustable head holder permanently attached to the operating table. The spindle carrier was independent of the head holder. The spindle was made vertical by means of built-in adjustments and levels. The head of the dog was made horizontal by means of a sterile level and a special support for it which fit across the supra orbital ridge of the skull, thus bringing the machine and the dog's head into alignment. From this point on the use of the instrument was very similar to the one first described.

CONCLUSIONS

A method has been described for the accurate placement of coagulating or stimulating electrodes in the hypothalamus of the dog. The technique may be used for the rhesus monkey as well.

REFERENCES

ATLAS, D. and INGRAM, W. R. Topography of the brain stem of the rhesus monkey with special reference to the diencephalon. *J. Comp. Neur.*, **1937**, *66*: 263-289.

BAILEY, P. and STEIN, S. N. *A stereotaxic instrument for use on the human brain. Studies in Medicine.* A volume of papers in honor of Robert Wood Keeton. Springfield, Charles C. Thomas, **1951**, pp. 40-49.

CARPENTER, M. B. and WHITTIER, J. R. Study of methods for producing experimental lesions of the central nervous system with special reference to stereotaxic technique. *J. Comp. Neur.*, **1952**, *97*: 73-132.

CLARK, G. The use of the Horsley-Clarke instrument on the rat. *Science*, **1939**, *90*: 92.

CLARKE, R. H. and HORSLEY, V. On a method of investigating the deep ganglia and tracts of the central nervous system (cerebellum). *Brit. Med. J.*, **1906**, *2*: 1799-1800.

CLARKE, R. H. and HENDERSEN, E. E. Atlas of photographs of sections of the frozen cranium and brain of the cat (felis domestica). *J. Psychol. v. Neurol.*, **1911**, *18*: 391-409.

CLARKE, R. H. Investigation of the central nervous system. Methods and instruments. *Johns Hopkins Hosp.* Special Volume. **1920**, 1-162.

[1] Designed by one of us (D. M. H.) in 1948 and constructed in the machine shop of the Harvard Medical School by F. J. Christensen.

CLARKE, R. H. and HENDERSON, E. E. Atlas of photographs of the frontal sections of the cranium and brain of the rhesus monkey (Macacus rhesus). *Johns Hopkins Hosp. Rep.* Special Volume. **1920**, 163-172.

COWIE, A. T. and HUME, D. M. Unpublished data.

GANONG, W. F. and HUME, D. M. Unpublished data.

GÉRARD, R. W., MARSHALL, W. H. and SAUL, L. J. Electrical activity of the cat's brain. *Arch. Neurol. Psychiat.*, Chicago, **1936**, *36*: 675-738.

HARRIS, G. W. The innervation and actions of the neurohypophysis; an investigation using the method of remote-control stimulation. *Philos. Trans. B.*, **1947**, *232*: 385.

HAYNE, R. and MEYERS, R. An improved model of a human stereotaxic instrument. *J. Neurosurg.*, **1950**, *7*: 463-466.

HESS, W. R. *Beitrage zur Physiologie d. Hirnstammes. I. Die Methodik der lokalisierten Reizung und Ausschaultung subkortikaler Hirnabschnitte.* Leipzig, Georg Thième., **1932**, pp. 122.

HODES, R., HEATH, R. G., FOUNDS, W. L. and LLEWELLYN, R. C. Implantation of subcortical electrodes in man by a stereotaxic method, in HEATH, R. G.: *Studies in Schizophrenia*, Cambridge, Harvard University Press, **1954**, 141-150.

HORSLEY, V. and CLARKE, R. H. The structure and functions of the cerebellum examined by a new method. *Brain*, **1908**, *31*: 45-124.

INGRAM, W. R., HANNETT, F. I. and RANSON, S. W. The topography of the nuclei of the diencephalon of the cat. *J. Comp. Neur.*, **1932**, *55*: 333-394.

JASPER, H. and HUNTER, J. A stereotaxic instrument for man. *EEG Clin. Neurophysiol.*, **1949**, *1*: 523.

JIMÉNEZ-CASTELLANOS, J. Thalamus of the cat in Horsley-Clarke coordinates. *J. Comp. Neur.*, **1949**, *91*: 307-330.

KRIEG, W. J. S. Accurate placement of minute lesions in the brain of the albino rat. *Quart. Bull. Northwestern U. Med. Sch.*, **1946**, *20*: 199-208.

MUSSEN, A. T. A cytoarchitectural atlas of the brainstem of the macacus rhesus. *J. Psychol. Neurol.*, **1923**, *29*: 451-518.

OLSZEWSKI, J. The thalamus of the macaca mulatta; an atlas for use with the stereotaxic instrument. Basel, Karger, **1952**, 93 pp.

RANSON, S. W. On the use of the Horsley-Clarke stereotaxic instrument. *Psychiat. Neurol. Bladen.*, **1934**, *38*: 534-543.

SACHS, E. and FINCHER, E. F., Jr. Anatomical and physiological observations on lesions in the cerebellar nuclei in macacus rhesus. *Brain*, **1927**, *50*: 350-356.

SAWYER, C. H., EVERETT, J. W. and GREEN, J. D. The rabbit diencephalon in stereotaxic coordinates. *J. Comp. Neurol.*, **1954**, *101*: 801-824.

SPIEGEL, E. A., WYCIS, H. T., MARKS, M. and LEE, A. J. Stereotaxic apparatus for operations on the human brain. *Science*, **1947**, *106*: 349-350.

SPIEGEL, E. A. and WYCIS, H. T. *Stereoencephalotomy (Thalamotomy and related procedures)*. Part I. Methods and stereotaxic atlas of the human brain. New York, Grune and Stratton, **1952**, 176 pp.

STELLAR, E. and KRAUSE, N. P. New stereotaxic instrument for use with the rat. *Science*, **1954**, *120*: 664-666.

TALAIRACH, J., HÉCAEN, H., DAVID, M., MONNIER, M. et DEAJURIAGUERRA, J. Recherches sur la coagulation thérapeutique des structures sous corticales chez l'homme. *Rev. Neurol.*, **1949**, *81*: 4-24.

TALAIRACH, J., DEAJURIAGUERRA, J. et HÉCAEN, H. Etude topographique des images ventriculaires en fonction des noyaux gris centraux. *Ann. Méd.*, **1950**, *51*: 83-100.

WINKLER, C. and POTTER, A. *An anatomical guide to experimental researches on the rabbit's brain.* Amsterdam, Versluys, **1911**, 40 plates.

WINKLER, C. and POTTER, A. *An anatomical guide to experimental research on the cat's brain.* Amsterdam, Versluys, **1914**, 35 plates.

Reference: HUME, DAVID M. and GANONG, WILLIAM F. A method for accurate placement of electrodes in the hypothalamus of the dog. *EEG Clin. Neurophysiol.*, **1956**, *8*: 136-140.

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FEUILLE DE CLASSEMENT DES EEG

L. L. Sorel, M.D.
Institut de Neurologie, Louvain, Belgique

(Received for publication: April 16, 1955)

Tout essai de travail scientifique dans un laboratoire d'EEG clinique, suppose avant tout l'utilisation courante d'un moyen simple et complet de classement.

Ce classement doit permettre de retrouver rapidement les affections de diagnostic identique et les tracés EEG qui présenteraient une activité électrique semblable.

Les fiches perforées, utilisées le plus communément ont certains désavantages qui les font abandonner par de nombreux laboratoires. Elles sont incomplètes, nécessitent une trieuse souvent très onéreuse et de plus demandent du temps pour les remplir correctement. Ces fiches doivent être anotées par une personne qualifiée, dont le temps est précieux. De plus l'établissement de la fiche perforée est un travail complètement indépendant du protocolage lui-même, et s'il en fait partie, allonge fortement celui-ci. Il arrive facilement enfin que lors de l'établissement ultérieur de la fiche il puisse s'y glisser des erreurs.

Ces différentes considérations nous ont incité à chercher un moyen de classification, qui puisse être complet, rapide et sûr à la rédaction, et facile à l'utilisation.

On utilise à cet effet une feuille ou fiche de description. Celle-ci est de format commercial classique, imprimée sur papier ordinaire. Elle est rangée d'après les numéros d'ordre des dossiers dans des classeurs standards.

L'énumération des diagnostics cliniques les plus courants rencontrés parmi les malades adressés au laboratoire d'EEG, et les cases destinées à noter l'âge des malades, font forcément partie d'une telle fiche, de même que nom, date du tracé et numéros du dossier.

Quelques cases au nombre de 9 donnent un aperçu d'ensemble sur le tracé.
En voici la signification:

N : Tracé normal
Lim: Tracé subnormal
1 : Tracé légèrement dysrythmique
2 : Tracé nettement dysrythmique
3 : Tracé gravement dysrythmique avec disparition le plus souvent de toute activité normale
4 : Tracé présentant des paroxysmes du type pointes-ondes
5 : Tracé présentant des anomalies localisées dans le lobe temporal
6 : Tracé présentant des anomalies localisées dans un autre endroit du cerveau que le lobe temporal
7 : Case à destination libre.

La particularité de la feuille consiste en la possiblité de décrire complètement chaque activité électrique notée au cours du tracé et les modifications que chacune d'elles subissent, sous l'influence des différentes épreuves.

La rédaction de la partie de la feuille destinée à cette description détaillée du tracé se fera suivant l'ordre logique du protocolage d'EEG.

Les premières questions posées seront: note-t-on la présence ou non de paroxysmes ? Les activitées continues ou paroxystiques sont-elles symétriques ou asymétriques ? Chaque colonne sera alors destinée à la description d'une activité électrique en notant la fréquence, l'amplitude et la localisation des ondes qui la composent, de même que la réponse de cette activité aux différentes épreuves.

S'il s'agit d'activité paroxystique on notera en plus divers détails descriptifs que l'on verra notés sur la feuille reproduite ici en exemple.

D'autres cases permettent de noter des renseignements complémentaires concernant l'évolution du tracé lors des contrôles ultérieurs ou la vérification éventuelle d'une tumeur à l'opération ou à l'autopsie.

Certaines nuances sont possibles. Entre une activité bilatérale d'une part et une autre activité strictement unilatérale d'autre part, il existe en effet une gamme de prédominances plus ou moins marquées. Cette gamme peut être rendu de la façon suivante: une légère prédominance gauche d'un côté, se marquant par une croix dans la colonne symétrique en face de prédominant à gauche. Une prédominance plus marquée sera notée par la description de l'activité dans les colonnes "asymétrie droite et gauche" en indiquant de plus une croix en face de prédominance à gauche dans les deux colonnes.

Si une crise électrique survient au cours du traçé la description de celle-ci n'est pas possible dans le détail. Une case permet de retrouver de tels traçés.

Le résultat de certaines épreuves ne peut pas non plus être décrit complètement. Il suffira de noter alors éventuellement en toutes lettres quel-

B..... Jacques
Nom:

Date: 12-7-54
N° 7.843

	Tracé de fond			Paroxysmes		
	Sym.	Asymétrie Dr.	Asymétrie G.	Sym.	Asymétrie Dr.	Asymétrie G.
1-2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13-24						
0 à 20 µV						
20 à 80 µV						
+ de 80 µV						
Uniqt						
Prédom.						
Prédom. à g.						
Prédom. à dr.						
Général						
Fronto-Frontal						
Frontal						
Central						
Pariéto-Occipital						
Temp. ant.						
Temp. post.						
Occ.						
Vertex						
Ond. isol.						
Ond. en tr.						
Pointes						
Pt. ondes						
Arceaux						
Rare						
Fréq.						
Synchr.						
Asynchr.						
Durée:- de 1 sec.						
1 à 4sec.						
+ de 4 s.						
R.A.Normale						
Incompl.						
Nulle						
ferm.y.f.app.						
ouv.y.f.app.						
Hyperpn. 0						
↗ fréq.						
↘ fréq.						
↗ ampl.						
↗ nomb.						
fait app.						
effet pr. apr.						
Cont.-Frayeur						
S.L.I.						
Cardiazol						
Sommeil						

N	Lim	1	2	3	4	5	6	7	Crise au cours tracé	Tum. contr.
		X				X				

Normal
Epilepsie — X
Syndromes psychiques — Hysterie, Nevropathie, Débilité mentale, Tics nerveux, Troubles caractériels, Psychose
Syncope
Traumatismes — Trauma récent, S.P.C.
Syndromes vasculaires — Hémorragie méningée, Hypertension sang., Thrombose, Spasmes, Ramollissement, Artériosclérose cérébrale
Syndromes infectieux — Méningite, Encéphalite, Arachnoidite, Méningo-encéphalite T
Tumeurs — Sus tentoriel, Sous tentoriel, Centro-médiane, Abcès, Hématome, Gliomes, Métastase, Kyste, Méningiome, Méduloblastome, Astrocytome, H.I.C.
Enfants — Encéphalite infantile, Spasmes du sanglot, Troubles de l'équilibre, Leuco-encéphalite, Enurésis, Hydrocéphalie, Arriération mentale, Arriération physique
Divers — Cephalées, Migraine, Mongolisme, Diplégie cérébrale, Choréo-athétose, Syndr. endocriniens, Eclampsie, Hypoglycémie, Narcolepsie cataplexie, Vertiges
Diagnostic non classé

F	M	0 6m	6m Ia	Ia 3a	3a 7a	7a 14	14 20	20 30	30 40	40 50	50 100	malade revenu M	sq.	Ag
	X							X					X	

ques mots, qui permettront de retrouver les sensibilisations interessantes.

Les avantages de ce moyen de classification nous paraissent prouvés.

La fiche est complète. Elle est purement descriptive et n'est de ce fait nullement stérilisante pour toutes recherches ultérieures.

Plus de 3.500 tracés ont été décrits jusqu'à ce jour dans notre service en utilisant une fiche semblable, sans que l'on éprouve une difficulté quelconque à ce faire pour quelqu'activité que ce soit.

La rédaction est rapide, non seulement elle n'allonge pas le temps du protocolage, mais lorsqu'on a l'habitude de l'utiliser elle arrive facilement à le diminuer. En effet les cases de la fiche sont disposées de telle sorte qu'au cours du protocolage on indique par des croix judicieusement disposées les moindres caractéristiques des activités enregistrées et la réponse de chacune d'elles aux principales épreuves exécutées d'une façon courante. La fiche de description une fois remplie sert d'aide mémoire, pour la dictée du protocole. La fiche peut aussi être remplie au préalable par une technicienne avertie et le médecin n'aura qu'à la contrôler en dictant les conclusions.

La rédaction est sûre, remplie par le médecin lui-même au moment de la lecture du tracé ou vérifiée par lui, il ne pourra se glisser aucune erreur dans l'établissement de la fiche.

L'utilisation de tel document est facile. Voici à titre d'exemple l'aspect d'une fiche décrivant le tracé d'un épileptique du sexe masculin âgé de 22 ans qui revient en contrôle:

Le tracé de repos est symétrique et montre une activité de base qui oscille en fréquence de 8 à 11 c/sec. en occipital des deux côtés et d'une amplitude voisine de 50 μV. En central et en temporal on note une dysrythmie de 5 à 7 c/sec. non survoltées. La réaction d'arrêt est normale pour les activités occipitales et incomplète pour les activités centro-temporales.

L'épreuve de l'hyperpnée accentue légèrement la dysrythmie occipitale et influence plus nettement l'activité centro-temporale, elle fait de plus apparaître des ondes monomorphes en trains synchrones prédominant en antérieur des deux côtés et dont la fréquence oscille de 3 à 4 c/sec. Ces activités sont survoltées. Ces paroxysmes ont une durée de 2 à 3 sec. environ, mais ils sont rares.

La sensibilisation cardiazolique a mis en évidence la présence d'un foyer d'anomalies lentes continues d'assez bas voltage (2 à 4 c/sec. $\pm$ 20 μV.) localisées uniquement dans la région temporale gauche. On note également prédominant dans cette région la présence de fréquents paroxysmes, brefs composés d'ondes d'une fréquence de 5 à 7 c/sec. mêlées de pointes et atteignant en amplitude 150 μV.

Cette fiche ainsi remplie est d'utilisation facile. Si l'on désire retrouver par exemple tous les tracés présentant des paroxysmes mêlés de pointes et localisés en temporal on compose une feuille de description en disposant la croix de telle sorte que les activités à rechercher soient seules représentées. On remet cette fiche à une secrétaire quelconque en lui demandant de retirer des classeurs toutes les feuilles qui contiennent, des croix disposées aux mêmes endroits. Elle pourra déjà opérer un premier triage en utilisant les 9 cases qui donnent un aperçu d'ensemble.

La recherche des feuilles de classement ayant le point commun désiré est plus longue que lors de l'emploi de fiches perforées. Seulement toute secrétaire même non initiée peut exécuter ce travail. Le temps d'une telle secrétaire est incomparablement moins précieux que celui du médecin qualifié.

Une fois le document retrouvé une partie du travail peut même être exécuté d'après la fiche de description vu son extrême précision.

Reference: SOREL, L. L. Feuille de classement des EEG. *EEG Clin. Neurophysiol.*, **1956**, *8*: 141-143.

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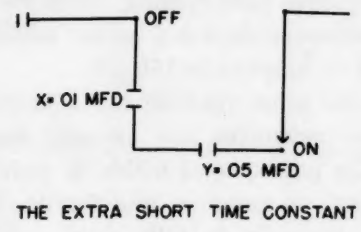
AN EXTRA-SHORT TIME CONSTANT FOR STUDY OF BETA AND GAMMA WAVES IN DEPTH RECORDINGS

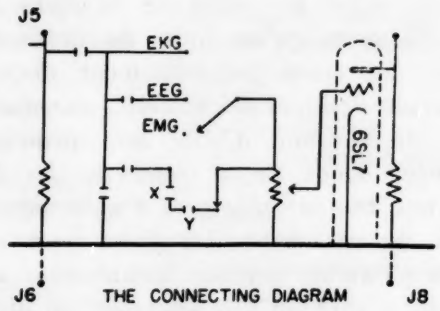
CARL W. SEM-JACOBSEN, M.D. and WILLIAM E. KUCHERA
Rochester State Hospital, Rochester, Minn.

(Received for publication: September 14, 1955)

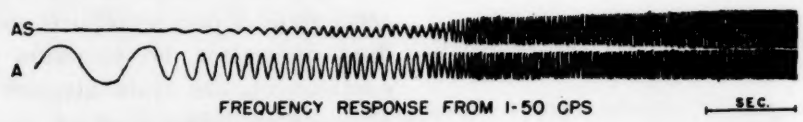
Considerable activity of beta and gamma frequency has been found in the course of depth recording from the human brain. To facilitate the study of these rhythms, various methods of filtering out the slower frequencies were tried. The EMG filter on the model III Grass electro-encephalographic instrument filters out only those frequencies less than 5 c/sec. We considered it necessary in addition to filter out frequencies up to 15 c/sec., as all this slower activity may mask the faster beta and gamma activity. This led to the development of what we have called the "extra-short time constant". The filters regulating the time constant are located before and after the second stage of the power amplifier in the Grass machine.



THE EXTRA SHORT TIME CONSTANT



THE CONNECTING DIAGRAM



AS=EMG+EXTRA SHORT TIME CONSTANT GAIN 7
A=EEG GAIN 6

DEPTH RECORDING DURING LIGHT STIMULATION

WITH & WITHOUT EXTRA SHORT TIME CONSTANT

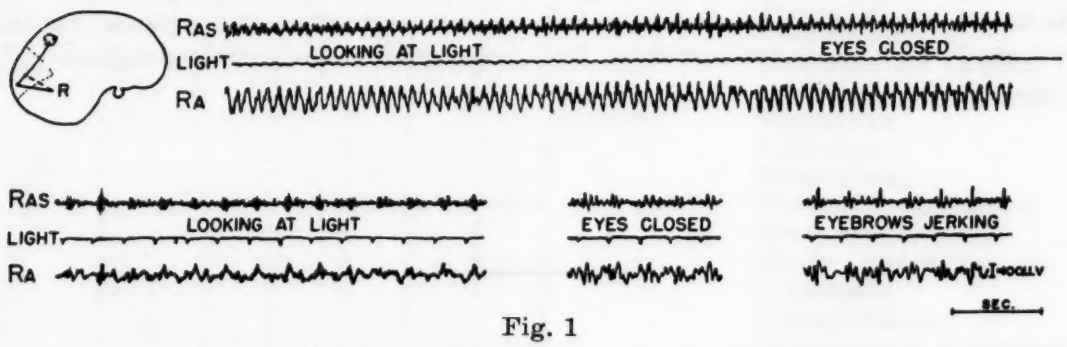


Fig. 1

Use of an extra-short time constant in depth electrography. Upper part of figure shows mounting of the constant and the frequency response when it is used. The lower part shows its effect on depth recordings.

The extra-short time constant has been mounted in the locations indicated in the accompanying figure in a model III B Grass machine as well as in a model III D.

Condensers are inserted in the circuits used when

the power amplifier is switched to the EMG filter.

A good filter was obtained when a 0.05-mfd. and a 0.01-mfd. condenser were placed in series, giving a combined value of 0.008 mfd.

The frequency response from 1 to 50 c/sec. is illustrated with a standard EEG filter and gain 6 in the channel labeled A, and with a standard EMG plus the extra-short time constant and gain 7 in the channel labeled AS. The increase of the gain in channel AS compensates for the decrease in the voltage of the response in the upper part of the beta-frequency band.

As most of the gamma rhythms so far recorded in the cerebral depths are of low to medium voltage, the increase of the amplification of these rhythms facilitates investigation.

The lower part of the figure illustrates details appearing in tracings from the depths of the occipital lobe during stimulation by light when the extra-short time constant is used. The pronounced difference in response when the patient looks at the light and when the eyes are closed is seen. In the first instance, bursts of fast activity are seen in response to each flash of light. These bursts, however, are clearly visible only in the AS tracings. Changes in electric activity, described in another paper (Sem-Jacobsen *et al.* 1956), at the onset of the photomyoclonic response and the jerking of the eyelids are seen when this filter is used.

REFERENCE

SEM-JACOBSEN, C. W., PETERSEN, M. C., DODGE, H. W., Jr., LAZARTE, J. A. and HOLMAN, C. B. Electroencephalographic rhythms from the depth of the parietal, occipital and temporal lobe in man. *EEG Clin. Neurophysiol.*, (in press).

Reference: SEM-JACOBSEN, CARL W. and KUCHERA, WILLIAM E. An extra-short time constant for study of beta and gamma waves in depth recordings. *EEG Clin. Neurophysiol.*, **1956**, *8*: 144-145.

A METHOD FOR EXAMINING ELECTRODES AND AFTER-DISCHARGES DURING ELECTRICAL STIMULATION

CARL W. SEM-JACOBSEN, M.D. and MAGNUS C. PETERSEN, M.D.
Rochester State Hospital, Rochester, Minn.

(Received for publication: October 10, 1955)

In the course of electrical stimulation of the brain by means of implanted electrodes, several questions have arisen. The most important of these are:

1. What happens in the vicinity of the electrode interface during stimulation ?

2. Are there breaks in the insulation caused either by faulty coating or by handling of the strands of leads ?

3. Are the waves recorded from the depths of the brain after stimulation produced only by neuronal activity ?

It was the last question that led to the development of the test to be described.

TECHNIQUE

A glass jar is filled with egg white and electrodes of the type used in the brain are inserted through a hole in the covering top plate. The egg white then takes the place of the brain and the jar with the plate represents the skull. The grounding of the preparation is done by sliding a small lead plate attached to the ground lead along the inner surface of the jar until it reaches the bottom. This ground plate is placed well away from the electrodes. For minute study, a single electrode is placed in a drop of egg white under the microscope. When several electrodes are used, a Petri dish containing the egg white with the electrodes inserted may be placed under a binocular dissecting microscope. This allows detailed study of the changes occurring around the electrode during and after electrical stimulation.

RESULTS

Several depth electrodes that have been used in human beings have been tested afterward by these macroscopic and microscopic methods. The resistance of the electrode is about the same in the egg white as it is in the brain.

Changes occur around the electrode during both unipolar and bipolar "stimulation". When the applied stimulus is strong enough, white clouds with small bubbles of air gradually appear around the negative electrode, while a brownish-yellow halo develops around the positive electrode. If the insulation is defective, these changes will appear around the faulty spots when the stimulus is applied. A further measurement of the strength of the insulation is made by increasing the voltage on the stimulator until the stimulus begins to break through the insulation. The use of faultily insulated electrodes for stimulation will result in the simultaneous unintended

stimulation of several portions of the brain, in addition to excitation of the part intended. This test of the electrode has been provoking as well as enlightening to several qualified workers. The test is of great importance, especially when wires as fine as 44, 46 and 52 gauge are used for electrodes.

The types of waves recorded after electrical stimulation are illustrated in the figure 1. Recordings obtained after electrical "stimulation" of egg white are seen on the left side. In this instance, the waves were recorded for more than 2 hours. When the waves no longer were discernible, the white clouds and the brownish-yellow halo around the electrodes had disappeared. This indicates that the changes produced by the applied stimuli were not irreversible but only temporary and probably of electrochemical nature. When the stimulus was below the threshold for the production of microscopic changes around the electrodes, slow waves were not encountered in the subsequent recording.

The appearance of high-voltage arrhythmic slow waves after stimulation may be used as a sensitive indicator of the level at which pronounced electrochemical changes in the brain around the electrodes will occur.

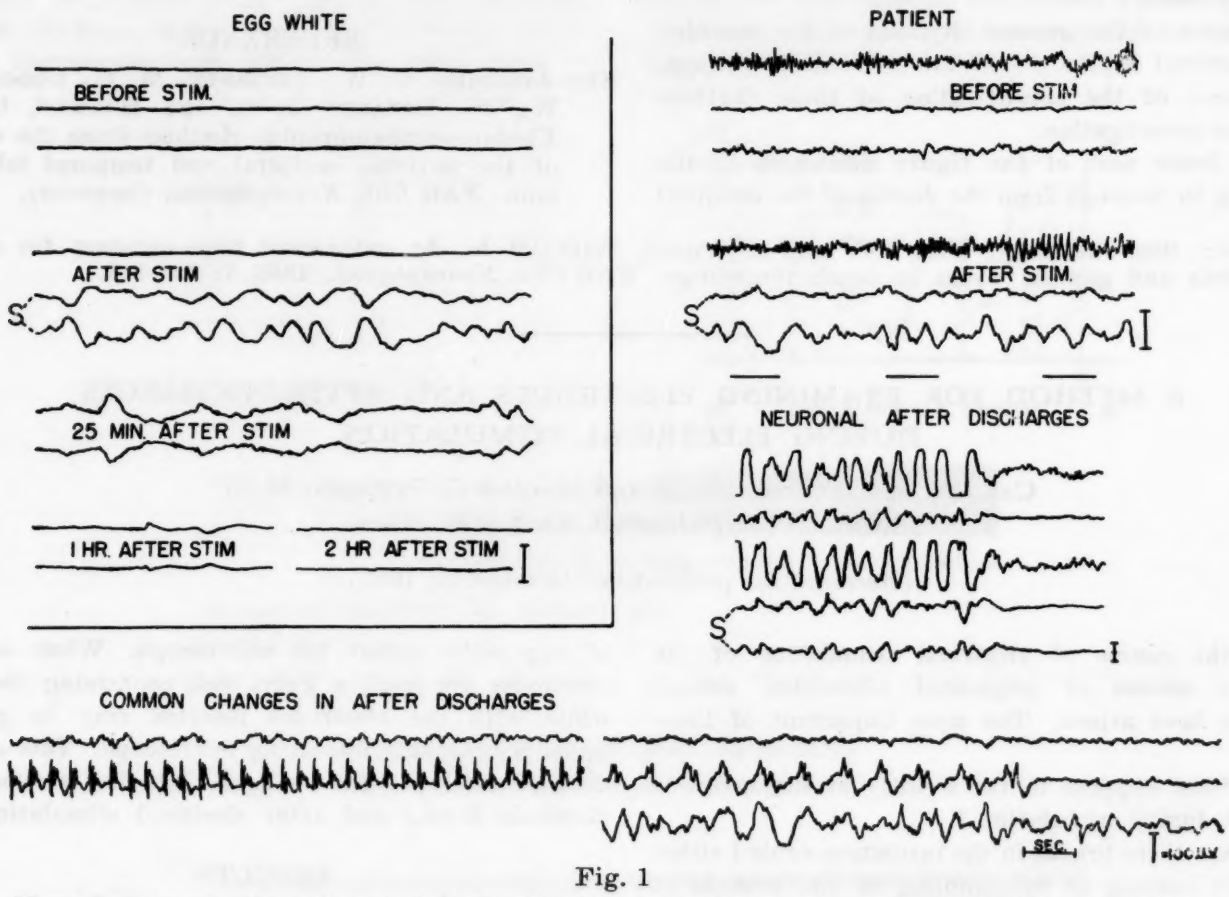


Fig. 1

Wave forms appearing after electrical "stimulation" of egg white (left) and after stimulation of the brain of a patient (right). The stimulus used was a square wave of the order of 2 to 4 V. and 1 mA., with a rate of repetition of 20/sec. and a train duration of 20 to 30 sec. Neuronal after-discharges in the brain frequently have been elicited with much weaker stimulation. The channels marked "S" indicate tracings from the electrodes through which the current was passed.
Same stimulus used in left and right column. Weaker stimulus used at the bottom parts illustrating neuronal after-discharges. Stimulus duration up to 20 msec.

Neither the visible changes around the contacts nor the slow waves appeared in the subsequent recordings when fluid electrodes, such as calomel electrodes, were used.

The authors express appreciation to Mr. Yanover, Buckeye Engineering Company, New York, for his time and interest in making the fine insulated stainless-steel wire.

Reference: SEM-JACOBSEN, CARL W. and PETERSEN, MAGNUS C. A method for examining electrodes and after-discharges during electrical stimulation. *EEG Clin. Neurophysiol.*, **1956**, *8*: 145-146.

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SOCIETY PROCEEDINGS

II CONGRESO SUDAMERICANO DE ELECTROENCEFALOGRAFIA Y NEUROFISIOLOGIA CLINICA

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Secretary of Honour: B. FÚSTER

I. ELECTRO-CLINICAL CLASSIFICATION OF THE EPILEPSIES

(Joint Meeting with the Uruguayan Society of Pediatriciens)

1. Electroclinical classification and limits of epilepsies in children. — F. ESCARDÓ, M. TURNER and N. TURNER, Buenos Aires.

In their paper the authors agree with Penfield and Jasper's definition, according to which the epileptic seizure is a ''state produced by an abnormal and excessive neuronal discharge within the central nervous system''. However, they state that this definition does not apply to all clinical cases, either from the pattern of the recorded discharge, or from its clinical expression. They point out that asthma, paroxysmal tachycardia, periodic vomiting and episodic behavior alterations are very often associated with abnormal and excessive neuronal discharges.

From a series of 676 cases (ranging from newborn to the age of 15), and according to clinical and EEG records they reach the following conclusions: convulsions are the least common manifestations of epilepsy in children because neuronal discharges can only occur at those levels of the central nervous system which have attained a sufficient degree of maturity; hence, clinical manifestations and EEG records of an epileptic child are not regular and uniform, but they do change constantly with the subject's development.

An analysis of 133 cases has led the authors to define the limits of so-called ''febrile convulsions''. The diagnosis must be made from the clinical and EEG point of view because it is impossible at first to know if fever and convulsions are only manifestations of epileptic discharge, or if they represent early symptoms of true encephalitis. Therefore, careful observation of febrile convulsion is required in order to discover their exact significance. In this way the authors found 83 per cent abnormal EEGs in cases of febrile convulsions.

The authors reported 31 cases of a definite syndrome: ''generalized flexion or extension epilepsy''. It is characteristic of early childhood and is accompanied by severe impairment of psychomotor development and a very abnormal EEG record (diffuse slow spike and wave complexes and multiple spike and wave complexes, ''hypsarrhythmia'' of Gibbs, or ''dysrythmie majeure'' of Gastaut).

Two forms of evolution were noted in ''generalized flexion or extension epilepsy'': (1) Towards cerebral palsy with mental retardation, and, (2) to a transformation into a myoclonic disorder.

The authors point out that ''generalized flexion and extension epilepsy'' should be regarded as a well-defined form of epilepsy. The epileptic discharge seems to take place on a ''postural level''. This is the only level which has attained a sufficient degree of maturity in children with extreme mental retardation.

2. Significado de las anomalías paroxismales y no paroxismales en el EEG de niños con problemas de conducta. — A. MOSOVICH y A. THOMPSON.

3. Estudios electroencefalográficos de 200 niños de edad escolar con trastornos de conducta y carácter. — E. TORRENTS y J. C. CHANS CAVIGLIA.

4. Familiar myoclinic epilepsy. Unverricht-Lundborg's disease. — J. GALEANO-MUÑOZ, R. ARANA-IÑIGUEZ and E. GARCIA-AUSTT, Montevideo, Uruguay.

Three cases of myoclinic epilepsy of the Unverricht-Lundborg type pertaining to three members of the same family are studied.

In three brothers now 13, 21 and 23 years of age respectively, the disease began between the ages of 11 and 12 with myoclinic jerks of the arms and legs. These troubles progressed at a rather rapid rate, becoming generalized before the first year after onset. In all the cases grand mal appeared at the age of 12 years. There has been a marked mental deterioration in all the patients with the progression of the disease.

The EEG in all three brothers shows similar changes: permanent slow waves, bilaterally synchronous, single and multiple spikes. Photic stimulation increases spikes, causing at the same time myoclonic jerks and transient unconsciousness.

Clinical and psychological examination of parents is normal. The father's EEG shows slow waves and bilateral random spikes. The mother's tracing is normal except for a myoclonic ocular response to photic stimulation of dubious interpretation.

The point of interest of this presentation consists in the fact that the father of these patients has a brother married to a sister of the mother. Three children were born to this couple, two of them being normal and the other, mongoloid.

5. Familiar myoclonic epilepsy. — J. B. GOMENSORO, B. FÚSTER, C. MENDILAHARSU, J. GALEANO y J. BOGACZ, Montevideo, Uruguay.

A family of epileptics consisting of six sons and the two parents were submitted to clinical, psychological and electroencephalographic examinations. The

latter were carried out with the patient awake and asleep and during hyperpnoea and photic-stimulation.

The father, 43 years old, had primary and hypnical grand mal crisis, and random myoclonic jerks up to the age of 9. Clinical and psychological findings were normal. The EEG only showed generalized bisynchronous discharges of high voltage, 3/sec. sinusoidal waves, during hyperpnoea.

Two daughters, 14 and 8 years old, had primary and hypnical grand mal alternating with or preceded by bilateral myoclonic jerks with flexion of the upper limbs or of the head. The EEG showed generalized bisynchronous paroxysmal discharges of spike and wave or multispike and slow waves. These discharges increased during hyperpnoea and photic stimulation. The latter also produced a clinical myoclonic response. Psychological tests showed a progressive psychic deterioration, especially marked in the 8 year old girl.

The mother and two daughters, 39, 19 and 10 years old, do not and did not have epileptic attacks, and their clinical and psychological examinations were normal. But the EEG showed non paroxysmal abnormalities in the posterior half of the right cerebral hemisphere.

A child of two years and a half, had grand mal crisis while suffering from rhinopharingitis. The EEG, which was negative for epilepsy, showed non paroxysmal activity of the same type as that shown on the mother's.

The 8 months old girl had normal clinical and EEG examinations.

The authors stress the fact that the epileptic members of the family have or had: (*a*) the same type of crisis; (*b*) the same type of EEG abnormalities, both suggesting the subcortical origin of the discharge; (*c*) mental deterioration, and (*d*) the absence of data suggestive of a symptomatic etiology, and the presence on the contrary, of data suggesting a genetic origin.

The non-epileptic members had an EEG negative for epilepsy, but showed non paroxysmal abnormalities localized in the posterior part of the right cerebral hemisphere.

The patterns of attacks and the EEG abnormalities suggest that these cases belong to the group of myoclonic epilepsies. The mental deterioration and the familial aspect point, among these, to the Unverricht type, even though these cases are not typical.

6. Crisis anartricas en epilépticos con foco situado sobre el área motora suplementaria. — V. Soriano.

7. Some correlations of clinical and EEG patterns in short seizures. — R. S. Schwab, Boston, U.S.A.

The correlations of the EEG patterns and clinical behavior are marked by some historical and classical milestones (mojons). The disappearance of the occipital alpha with opening of the eyes described in 1928 by Berger and the spike and wave of petit mal by Gibbs in 1935 are the most brilliant examples. The petit mal is a neurological entity — an absence or lapse of consciousness of 2 to 15 sec. with only staring — flicker of eyes, no other motor movements. Some lapses grow by spread to other brain areas, and then cause simple or complicated motor acts, persist for minutes to even hours with spike and wave in the EEG and are no longer petit mal (classic) but short focal or psychomotor seizures.

The film using a split frame technique illustrates this.

The details of how the patient and the EEG tracing can be photographed on the same film will not be described here. The November 1954 EEG Journal has this described in detail.

The film shows first a patient who for 7 seconds has a simple staring petit mal and then it spreads to the motor area producing bilateral facial twitches. The whole attack lasts 24 sec. The second patient was first filmed in 1938 by a more tedious and complicated technique and shows a spike and wave discharge with a simple stare for 8 sec. — then this spreads to the temporal lobe producting the typical chewing movements of the automotism of the psychomotor seizures which lasts 20 sec. Two movies taken in 1955 will be presented showing the same patient with wave and spike discharge and chewing movements during the attack. The last film shows hysterical seizures in a conscious patient, with only artefact in the EEG.

The purpose of the film is to show that the spike and wave can also be found in short automatisms as well as in simple petit mal.

8. Aporte del electroencefalograma de la base en la clasificación electroclínica de las epilepsias. — Alejandro P. Arellano, Lima, Perú.

La técnica electroencefalográfica para los registros de la base, usando los electrodos nasofaringeales y timpánicos, permite una exploración bioeléctrica mejor de las neuroestructuras vecinas a la base craneal, especialmente las del sector basilar del rinencéfalo. Pues con esta técnica los electrodos basales emplazados se encuentran mucho más cercanos al rinencefalón que con cualquiera otra de las técnicas hasta hoy empleadas en cráneo intacto. Dentro de los "patterns" electroencefalográficos descritos para determinadas epilepsias, tal vez en el grupo de las epilepsias parciales denominadas psicomotoras, podría distinguirse un sub-grupo por sus características eléctricas más evidentes en el trazado de la base. La descarga eléctrica sería de escasa irradiación o con una definida irradiación especialmente temporal y que aparentemente tiene una interpretación neurofisiológica. Esta correspondería propiamente a las epilepsias rinencefálicas.

9. A new electroencephalographic rhythm. The alpha paroxysmal rhythm. — Aldo Imbriano.

10. Unilateral conscious myoclonic crisis simulating a cephalic tic. — J. R. Marcos and B. Fúster, Montevideo, Uruguay.

A film and the EEG records were shown as a complement of the clinical report of a 11 years old boy who since age of 8 and a half showed clonic jerks of the head to the right and forward. These jerks, which were repeated at a frequency of 3-4/sec. in bursts of 1-2/sec. duration, occurred several times a day. Until the consultation, they were considered to be a manifestation of cephalic tic.

Family and personal history were normal, except for an unimportant head trauma. Neurological, radiological and eye examinations were normal. The psychological tests showed only an emotional instability and an inferiority complex because of his fits, which strengthened the diagnosis of cephalic tic. However,

the EEG showed ictal paroxysmal abnormalities of great interest, because they were constituted by bursts of 3/sec. spike and wave recorded over the whole hemisphere contralateral to the side of the clonic jerks of the head. The latter were synchronous with the spikes of the spike and wave complexes.

Three to four Mysoline tablets a day (1-0.750 gm.) made the spontaneous crisis disappear, but an EEG made three months later still showed paroxysmal bursts of the same type, while hyperpnoea provoked a clinical response by then reduced to a contraction of the triangularis labii and mentalis muscles of the face.

The cortical or subcortical origin of the epileptic discharges producing this sort of attack is discussed.

11. Clinical correlates of 14 and 6 per second positive spikes (1865 cases). — Frederic A. Gibbs, Chicago, U.S.A.

The clinical investigator has two responsibilities: (1) to gain significant information and (2) to convince others of its significance. Failure to perform the second function reduces the value of the first. The facts about the 14 and 6 per sec. positive spike discharge are essentially as we stated them ten years ago as we presented them in the second volume of the Atlas. What we have now is the emphasis and detailed delineation of the major correlates of this pattern that can be made out from an analysis of 1865 cases.

The first five slides show pure examples of these patterns. Usually the discharge is most clearly seen in the temporal and occipital areas, in light sleep. It is very rarely seen in the waking state. In some cases other complicating types of epileptic disorder are present (slide 6). These mixed cases have not been included in the present series. The discharges are usually bilateral but independent in the left and right hemispheres (slide 7).

Most usually the two patterns, 14 and 6 per sec. positive spikes, are found together (slide 7). Fourteen per sec. positive spikes are slightly commoner in children and 6 per sec. in adults. Only one third of the cases are sent in with a diagnosis of epilepsy (slide 8). The commonest major complaint is "pain" (slide 9), next convulsions, and next dizzy spells. Pain is the commonest aura (slide 9). Epileptic seizures when present are most often of the grand mal type (slide 10). But many kinds of bizarre seizures are encountered of special social importance are rage attack for these sometimes result in homicide.

These patterns occur in a fraction of a per cent of normal control above 15 years of age (slide 11). Their higher incidence in younger children is for the most part due to a refusal to take the complaints of pain, dizziness, rage, etc. in children seriously.

The commonest etiology is trauma (slide 12). Usually concussions without brain laceration when produced by tumors are in or impinge upon the thalamus or hypothalamus (slide 13).

This type of disorder is one of the commonest forms of epilepsy and is often not diagnosed or misdiagnosed. Monopolar sleep recordings are of great value for its diagnosis.

In general it responds more readily to anticonvulsant medication than any other type of epilepsy. It is chiefly a disorder of adolescents and young adults and may lead to suicidal tendencies with increasing age.

12. Conscious adversive seizures of subcortical origin. — B. Fúster and C. Castells, Montevideo, Uruguay.

The authors reported two patients with primary conscious adversive seizures, not preceded by any conscious motor, sensitive (somatic or vegetative) or psychical phenomena.

In both cases, the interictal EEG showed generalized bisynchronous paroxysmal discharges of 3 per sec. spike and wave, and multispike and wave rhythm. In one of them the seizure provoked by photic stimulation was filmed.

In spite of the fact that the seizure was lateralized and that in one of the patients the conjugate deviation of the head and the eyes continued with turning of the trunk, the paroxysmal discharges on the EEG continued perfectly symmetrical and synchronous.

The probable origin of the epileptic discharges in these cases is discussed.

13. The localization of spike seizure activity and the spread of seizure discharges in the depth of the brain of patients with psychomotor epilepsy and with schizophrenia. — J. Kendrick and F. A. Gibbs, Chicago, U.S.A.

14. The electroencephalogram in surgical epilepsy. — C. Marshall and E. A. B. Walker.

15. Further experiences with the selection of drugs by means of the EEG. — Tracy J. Putnam, Los Angeles, U.S.A.

In recent years, the rapid increase in the number of drugs available has created a new problem, namely, the selection of the best drug for the individual patient. Each drug available is capable of keeping some patients seizure-free and also of making some patients worse. Usually 2 to 3 months is required to evaluate each drug and the delay may be disastrous.

For the past 5 years, the author and his co-workers have employed a rapid method of selection in difficult cases. The patient is usually hospitalized for about 2 weeks and given each morning a large dose of a different anticonvulsant. For example, 1.0 gram of phenobarbital is given one day, 1.0 gram of diphenylhydantoin the next, 1.0 gram of Mesantoin the next, and so on. Each day about the time that the medication has been absorbed, an EEG is taken. When all medications have been used the records are compared. It is usually clear that some of them increase the EEG abnormalities, some decrease them. Uniformly, the drugs which have an adverse effect on the record are poorly tolerated and ineffective, but this is rarely true of those which do well in the test.

If no drug can be found which keeps the patient seizure-free, the use of the intensive or narcosis treatment is usually advisable.

16. Evolución clínica y electroencefalográfica de enfermos con tratamiento medicamentoso. — A. Mosovich y A. Eurnekian.

17. Prolonged psychic disturbances in epilepsy. — F. Ramírez, E. García-Austt and H. Garbarino, Montevideo, Uruguay.

Psychic manifestations of epilepsy may be divided into: (*a*) ictal manifestations, lasting only few in-

stants; (*b*) prolonged manifestations, lasting hours, days, weeks or even months. This second group also corresponds to a double expression:

(1) Prolonged psychic manifestations of true epileptic nature which we distinguish as crepuscular states as a whole (mental confusion, automatisms, dreamy state, epileptic mania, stupor, etc.). A state of altered consciousness is a common characteristic of all these conditions. Their prominent features are: the tendency of the seizures to come in bouts, their rapid onset and disappearance, the recurrence of the same clinical picture, amnesia and their good response to antiepileptic drugs. In these cases EEG changes are exclusively or predominantly located in the temporal lobe, unilateral or bilateral. Half of the cases show permanent changes of the lesional type.

(2) Epileptic psychoses (mania, melancholia, deliria, etc.). In these instances there are EEG changes of epileptic nature even in subjects with no clinical epilepsy. To rule their epileptic origin it is necessary to find at least two of the features listed in the previous group.

18. Manifestaciones clínicas ictales en sujetos con focos epileptógenos interictales en regiones cerebrales clínicamente mudas. — B. Fúster, J. Bogacz, J. J. Viñoles y Castells, Montevideo, Uruguay.

19. Electroclinical classification of epilepsy. — E. Garcia-Austt, L. Pérez-Achard and C. Galeano Muñoz, Montevideo, Uruguay.

It is not possible to make an "electroclinical" classification of the epilepsies. There is only one well-defined electroclinical entity, the petit mal, but even this may be criticized. Thalamic epilepsy, temporal epilepsy, rhinencephalic epilepsy and so forth, are only electroanatomical classifications, most of them being purely hypothetical.

The authors feel that a more suitable classification of epilepsy should be based on electroencephalographic as well as on clinical criteria. However, it is rather difficult to correlate both of them because electroencephalographic data are not always consistent with the clinical picture. When a well defined EEG pattern is taken into consideration one may find that it corresponds to different clinical conditions. On the other hand, the same type of seizure in different patients may have different electrographic expressions.

Most cases of epilepsy can be classified from a physiopathological point of view after the patients have been thoroughly studied. It seems therefore, to be more accurate to speak of a physiopathological classification of epilepsy according to the initial location of the discharge. Two main groups can thus be defined: epilepsies consecutive to discharge in one or more focal corticothalamic systems and epilepsies consecutive to discharge in one of the diffuse projection systems.

20. Estudio comparativo de la clínica y la electroencefalografía en la epilepsia. — V. Soriano.

II. METHODS OF ACTIVATION OF THE EEG

21. The use of 4560 R P in electroencephalography. — P. Pinto Pupo, E. Zukerman, Rosa Helena Longo, Sao Paulo, Brazil.

The authors have used the 4560 RP (Rhodia Laboratories) intramuscularly, in doses of 25 mgr., and have analysed the results according to its influence: (*a*) in the basic electrical activity of the EEG, (*b*) in the activity of epileptogenic lesions, and (*c*) in the patient's sedation, mainly in those patients who presented emotional tension or anxiety, or, who were uncooperatives.

The authors found that the drug does not have any influence on the basic rhythm of the EEG record, nor in the activity of epileptogenic foci; as sedative, the drug has presented different results which are not yet conclusive.

Since the drug does not affect the basic record or the epileptogenic activity, it can be used as coadjuvant in the routine EEG of patients suspect of being epileptics.

22. La aminopirina intravenosa como activador del electroencefalograma. — Juliao de Freitas, Paulo Adail y Vaz de Arruda, Brazil.

23. The effect of Reserpin on the scalp and basal electroencephalogram. — Alejandro P. Arellano y Raul Jeri, Lima, Perú.

There is very little information in regard to the electroencephalographic changes produced by Reserpin. Basal electroencephalographic on this subject have not been done so far.

In this preliminary presentation the authors show their first results of an investigation of the effects of Reserpin upon the electroencephalogram. Two tympanic and two pharyngeal leads were used for the basal electroencephalogram, as it has been described by one of the authors. For scalp recording the standard technique was used; 9 patients were selected, 2 normals for control, 5 subjects with a definite abnormal brain wave pattern (2 petit mal, one grand mal), one psychomotor with temporal spikes, one psychomotor with abnormal basal electrogram and 2 subjects with psychoses. From this small series, it appears that Reserpin produces or increases moderately the delta and theta activity and activates seizures in petit mal and grand mal epilepsy. It is interesting that these slow waves replace or are intermingled with the primary spike activity in psychomotor epilepsy especially at the base. In this type of seizure the activating effect is therefore not so clear. The epileptic condition in these cases improves when the Reserpin is associated with anticonvulsant drugs.

The authors discuss the possible mode of action of Reserpin, suggesting that this drug may act on rhinencephalic mechanisms involving neuronal circuits which Papez considered as the possible basis for emotional processes.

24. Electrophysiological and clinical aspects of "neurolysis" and artificial hibernation. — E. Bérard and M. Turner, Buenos Aires, Argentina.

Changes in several electrographic records (electroencephalogram, electrodermogram, electromyogram) sudoration test (adrenalin test), and changes of the skin temperature provoked by the slow and i.v. injection of 25 to 50 mgr. of chlorpromazine were reported by the authors. Investigations were carried out on

8 subjects with normal EEG, 21 epileptics, 5 neurotics with activated pattern (desynchronised), 2 psychotics and 1 post-encephalitic hemi-Parkinsonism.

Continuous EEG records of 5 psychotics submitted to artificial hibernation therapy with refrigeration and hypothermia (29 to 30 C. degrees) over 3 to 4 days, were also considered.

The methods and the findings were reported and discussed and the following conclusions were drawn:

1. In man chlorpromazine produces a state of relaxation and at the same time a greater synchronisation in the normal EEG record; in the "activated pattern" (desynchronised) of neurotic subjects a synchronisation with appearance of the alpha rhythm is observed. In epileptics an activation of paroxysmal episodes in the following cases was obtained: (*a*) patients with low photic-Metrazol threshold; (*b*) in the patient with paroxysmal bursts of bilateral and synchronous spike and polyspike-and-wave, 3 c/sec.; and (*c*) in the temporal epileptic cases with unilateral or bilateral simultaneous or independent focus.

During artificial hibernation the morphology of EEG is not the same as that of sleep; three phases were possible to describe: (*a*) a very important disorganisation at the beginning of hibernation; (*b*) secondary stability, and (*c*) quick awakening. The reactivation of the EEG record to the psychosensorial stimuli, is very attenuated. However, it may persist for the very strong ones, or for those stimuli charged with affective value. Morphology and reactivation are practically independent of the central temperature of the patient.

2. Chlorpromazine inhibits the electrodermographic response to the sensorial, affective and nociceptive stimuli.

3. Chlorpromazine diminishes the involuntary electromyographic activity (neuro-muscular tension, trembling, tics, etc.).

4. Chlorpromazine produces an inhibition of the adrenergic sudoral response of central origin.

5. Chlorpromazine causes an approximation of the skin temperatures of the distal and proximal segments of the body, through the inhibition of the central mechanisms of vasomotor regulation.

All these changes may be explained by the central action of the drug, specially upon the brain stem reticular formation.

25. Myoclonic reflexes exaggerated by startling stimuli. (Film). — C. Castells and B. Fúster, Montevideo, Uruguay.

The authors report the case of a patient 29 years old, who since the age of fifteen showed conscious myoclonic jerks provoked by auditory, visual or tactile stimuli having a startling character. The jerks were bilateral, symmetrical, generalized to all the skeletal muscles and sometimes associated to a lateral deviation of the body as if trying to avoid an aggression. The jerks were conscious but involuntary, and so sudden as to throw down objects held in the hands.

The EEG was negative for epilepsy, in waking state, during hyperpnoea, photic stimulation, induced sleep and Cardiazol activation (400 mgr., Merlis technique).

The neurological examination was normal. The familial and personal history was negative for epilepsy, but on the contrary, there were a number of findings in favour of the neurotic nature of the disorder.

The patient, who had not improved with antiepileptic medication did remarkably well on chlorpromazine.

The physiopathological mechanism of this kind of disturbance is discussed, as well as the probable participation of the reticular system.

26. Primary conscious adversive seizures precipitated by startling stimuli. — B. Fúster and J. R. Marcos, Montevideo, Uruguay.

The authors report a case of symptomatic focal motor epilepsy with primary conscious adversive seizures to the right. These seizures were easily elicited by any kind of stimuli, visual, auditory or tactile, having a startling character. There was adaptation to the same or other kinds of stimuli when repeated, and when the patient was aware that the stimulus was coming.

The interictal EEG showed non paroxysmal abnormalities over the posterior two thirds of the right cerebral hemisphere, and paroxysmal activity over symmetrical regions.

The ictal EEG only showed generalized bisynchronous paroxysmal discharges of spiky waves of varying frequencies according to the intensity and duration of the seizures.

The patient had serious behaviour disturbances which were not controlled by medical treatment.

The relationships are discussed between this case and the others reported by one of the authors in the preceding paper.

27. Clinical and EEG changes accompanying variations in glycemia. — J. Bogacz, C. Rabelo, B. Fúster and J. J. Viñoles, Montevideo, Uruguay.

A revision was made of all publications from 1929 to 1954 on the clinical and EEG changes accompanying variations in glycemia.

In normal persons, even during the pre-convulsive stage of insulin hypoglycemia, there were EEG changes: a slowing down of the frequencies which became more pronounced (appearance of diffuse delta waves) as the convulsive stage was approached. In none of them was focal or generalized epileptiform activity seen. On the contrary, in the group of reports of the EEG of epileptics, it was shown that insulin hypoglycemia is a specific activating mechanism. It activates 100 per cent of cases of petit mal, even those with a negative response to voluntary hyperpnoea (Gibbs, Gibbs and Lennox 1939), it increases previously existing epileptiform activity, even of focal type, and provokes the appearance of epileptiform abnormalities in 80 per cent of epileptics having a normal EEG (Baisset *et al.* 1948).

The most important conclusions reached from this revision are: 1) Insulin is an activator of almost specific interest, at least in epileptics; 2) it is effective in all or nearly all cases, according to the clinical or EEG type of epilepsy; 3) it produces very slight clinical effects upon the patient, and with appropriate doses never provokes a generalized convulsive crisis; 4) the technique is simple (1 unit per 4 kg. of body weight, intravenously).

28. The methods of electroencephalographic activation in the diagnosis of the epilepsies. — Aldo E. Imbriano.

The following methods of activation are studies comparatively in a total of more than ten thousand EEG examinations on 3,000 epileptics: hyperpnoea,

intermittent photic stimulation, auditory stimulation, drugs, and combinations of these activating procedures were used.

Voluntary hyperventilation amounting to an exchange of 30-45 liters per min. and ± 20 respirations per min. was carried out during 3 min.

Intermittent photic stimulation was carried out, using light flashes produced by a stroboscope. Its diagnostic efficiency in childhood epilepsy has been demonstrated. In adults this activation method is less efficient.

Auditory activation with repetitive stimuli produced by an electronic device is less effective but proved valuable in the study of conditioned reflexes.

The pharmalogical methods tried were numerous: caffein, hydration with water alone, and water combined with Pitressin, Pitressin, strychnine, morphine, insulin, Cardiazol (Metrazol) amphetamine. The rapid intravenous injection of 200 mg. of Metrazol has been used as done by previous investigators, and it was verified that it stimulates the epileptics without affecting normal individuals.

Amongst the methods of *combined activation* were used: *photo-Metrazol stimulation,* Gastaut (1949-1950); *photic stimulation with hyperventilation,* this gave good results in the diagnosis of lesser epileptic manifestations; *photic stimulation combined with the ''stroboscope'' phenomena,* this was used to provoke paroxysmal delta dysrhythmia. The ''stroboscope'' phenomenon is produced when the patient moves his fingers or the hand in front of the stroboscope.

From our experience, we think that the best method to use and which gives the greatest percentage of positive results, is that of *hyperpnoea* practised with a 20/min. respiratory frequency, a good respiratory amplitude for a duration of 3/min.

29. EEG changes during hyperpnoea. A critical review of the bibliography from 1935 to 1955. — J. J. Viñoles, C. Rabelo, B. Fúster and J. Bogacz, Montevideo, Uruguay.

A revision was made of the literature available for the 20 years from 1935 to 1954 so as to re-assess the previous results, by means of the present-day knowledge of the classification of epilepsies, and by means of the standards of abnormality for the interpretation of the EEG.

Conclusions.

(1) The results are far from uniform, because hyperpnoea has not been used according to a standard technique which would allow the results to be compared.

(2) In assessing the EEG results, specific changes must be separated from the non-specific. Only specific changes are significant. Among these, the most frequent is the spike and slow wave of 3 c/sec., seen in 85 per cent of patients with petit mal (Gibbs, Gibbs and Lennox).

No complete statistical study has been made of the other specific changes, nor of their occurrence in various types of cortical or subcortical epilepsy.

(3) Although, statistically, there is a higher percentage of non-specific changes in epileptics, in any given case one cannot say whether it is epilepsy or not, hence these changes are valueless for diagnosis.

(4) Among the factors which influence the response to hyperpnoea, especially the non-specific, the most important are the age of the subject and the blood sugar level.

30. Effect of photic stimulation in the visual pathways and cortex of the cat. — Donald B. Lindsley.

Response have been recorded simultaneously in several stations along the visual pathways, including the retina, optic tract, lateral geniculate, optic radiation, cortex and superior colliculus. These have been studied relative to various stimulus parameters such as frequency of flash, flash duration, light-dark ratio, intensity, and wave-length. The results throw light upon visual fusion, wave-length differentiation, and other aspects of the visual process, but also bear upon the mechanism of photic activation and photic driving.

31. Photic stimulation in infancy and in photo-epileptic children. — Donald B. Lindsley.

Photic driving effects have been demonstrated in young infants before the establishment of spontaneous alpha rhythms. In photo-epileptic children different wave-lengths have been found which are selective for the production of seizure discharges. These results will be discussed in relation to experimental results in animals.

32. The relationship of single, paired and serial stroboscopic flashes to the degree of occipital response in the EEG in various clinical states and in normals. — R. S. Schwab, A. England and M. Grey, Boston, U.S.A.

33. La activación fótica. Valor comparativo con la hiperventilación en las diversas formas clínicas de la epilepsia. — A. Mosovich.

34. Fotoestimulación e hiperventilación combinadas. — L. Levit.

35. Musicogenic epilepsy. — R. G. Bickford.

In summary, this was a 23 year old girl, who had a history of attacks of confusion brought on by music. Only the rather exotic kinds of jazz music were effective stimuli. In the attack she showed lacrimation, salivation, swallowing movements, and each attack was followed by a typical aphasia. This is well shown in the movie. Her resting and sleep EEG showed only minimal abnormalities, these being most marked in the left Sylvian and temporal area. During the seizure as you will see in the slide, there is the usual diffuse rhythmic 4-6 per sec. activity together with some muscle and eye movement artefact. In this particular seizure, the recording from the right temporo-frontal area was analyzed and the increase of theta as the seizure progresses is clearly seen. There seems to be no definite lateralization of the discharge during the seizure. However, the occurrence of aphasia following the attack clearly indicates that the left temporal lobe and adjacent areas are involved. As many as six seizures were induced in the laboratory by stimulation with jazz music. Other auditory stimuli, such as repetitive clicks, and other beat frequencies were unsuccessful in inducing a seizure. An air study, which was carried out, was negative, showing normal ventricular patterns, and in view of the fact that the focus was probably in the dominant hemisphere and aphasia was a constant feature of the attacks, it was decided that she was not a suitable candidate for a surgical excision. In view of the marked psychiatric components, long term psychotherapy was carried out over a period of nine

months. While the psychiatrists were confident that the combination of psychotherapy and anticonvulsant treatment had resulted in considerable improvement, in the laboratory it was still possible to produce attacks by musical stimulation, and little change in threshold was noted.

36. La activación con barbitúricos en el examen EEG de los niños. Comparación entre las modificaciones eléctricas bajo el Nembutal y el Seconal sódico. — A. Mosovich.

37. The asymmetry of the "K" complexes in focal epilepsy. — J. J. Viñoles and B. Fúster, Montevideo, Uruguay.

An electroencephalographic study was made, during Nembutal induced sleep, of 10 persons presenting clinical and EEG manifestations of focal cortical epilepsy, and 10 presenting subcortical epilepsy. The K complexes studied, were obtained by various auditive stimuli such as a clap of the hands or a well defined note of 100 c/sec.

In focal epilepsy, evident asymmetry of the K complexes was observed, which in the focus, and sometimes in a wide area around it, showed a greater amplitude and duration of the slow component, as compared to that from the corresponding area on the other side.

We believe that the difference between these results and the depression of the K complex usually seen in diseased areas, can be explained by taking into account the fact that in the cases we studied, the lesions were electroencephalographically unimportant. The latent hyperexcitability present in the epileptogenic focus, would thus be able to give a more synchronized response to the subcortical stimuli responsible for the secondary response.

The K complex, which is a secondary response to sound stimuli, is facilitated in the same way that the primary response is in the potentials arising from the latent hyperexcitability in the epileptic focus, but besides, the cortical synchronization during sleep facilitates a more synchronized manifestation of the response.

38. Value of natural or induced sleep in the electroencephalogram. Results of 500 observations in patients with convulsive disorders. — Doris Sailer Albernaz and Jośe Geraldo Albernaz, Belo-Horizonte, Brazil.

Sleep was induced with small amounts of Seconal or Dormison or was obtained naturally in 97.8 per cent of the patients.

Five hundred patients with history of convulsive disorders in whom sleep records were obtained, constitute the basis of this study. In 25.8 per cent of the tracings the pattern were normal, with the patient both awake and asleep. In 22 per cent of the cases there were abnormalities only during wakefulness and in 11.6 per cent only during sleep. In the remaining 40.6 per cent there were abnormalities both in the waking record and in the sleep tracing. In this last group, of 203 cases, both types of records showed the same kind of abnormality in 73 cases, but in 130 cases the abnormalities found during sleep were entirely different from those found in the record of the wakeful patient. Therefore, sleep demonstrated abnormalities not found during wakefulness in 37.6 per cent of the entire series.

It was also noticed that paroxysmal seizure discharges were most common during sleep and that slow wave foci and paroxysmal slowing were more easily detected during wakefulness.

39. La activación cardiazólica en las epilepsias temporales (film). — B. Fúster, J. J. Viñoles, J. Bogacz, J. Otegui y C. Castells, Montevideo, Uruguay.

40. Activación fotometrazólica en las epilepsias. — C. Villavicencio, Santiago, Chile.

41. La activación metrazólica del EEG. — E. Bancalari.

42. Algunos resultados de nuestra experiencia con activación cardiazólica. — Sergio Ferrer Ducaud.

Se hace una breve revisión de los trabajos en los cuales se ha empleado el Cardiazol bajo registro electroencefalográfico. El material está constituído por 81 sujetos de los cuales 55 son epilépticos y 26 ''funcionales''. Los epilépticos se agrupan en: A. Con netas manifestaciones en el reposo y durante la hiperventilación (38) y B. Con trazados normales o en el límite de la normal (17).

Se emplea el método de inyectar 50 mgr. cada 30 seg., hasta llegar en lo posible a la activación clínica. Se analizan las razones que justifican esta actitud.

Se analiza el diferente comportamiento de los epilépticos que en el reposo presentan descargas síncronas y bilaterales con el de aquellos que exhiben una disrritmia difusa y con los que muestran una epilepsia focal. Se demuestra en este último grupo que el 77 por ciento se activa eléctricamente y sólo el 66 por ciento clínicamente, con una dosis promedio de 441 mgr.

Se estudia comparativamente el grupo de los enfermos ''funcionales'' con el de los epilépticos sin manifestaciones en el reposo. Se obtiene que con una dosis de 300 mgr. o menos el 75 por ciento de los epilépticos alcanza la dosis convulsiva, en tanto que sólo 7 por ciento de los funcionales.

Se establece que no hay diferencia significativa en el umbral convulsivante de individuos entre 10 y 15 años y por encima y debajo de los 20 años.

Se estudian los porcentajes con que alcanzan la crisis convulsiva a dosis ascendentes de Cardiazol, las epilepsias generalizadas, focales y los enfermos ''funcionales''.

Se demuestra que el umbral del primer paroxismo no tiene la especificidad del fenómeno convulsivo crítico y que la dosis con que ocurre éste da la mas alta probabilidad de diferenciar si un fenómeno es o no comicial.

Se compara el umbral mioclónico con el umbral convulsivante y se establece que ambos no ascienden de manera paralela y que en el 57 por ciento de los casos se puede evitar la crisis convulsiva deteniendo la inyección en la dosis mioclónica.

Finalmente se examinan 13 epilepsias ''psicomotoras puras''. El Cardiazol reproduce en 6 la crisis clínica, en tres desencadena un fenómeno automático preconvulsivo y en 4 sólo determina una crisis convulsiva.

43. Metrazol activation in epilepsy. — L. Pérez-Achard, E. Garcia-Austt and C. Galeano-Muñoz, Montevideo, Uruguay.

A large variety of techniques of Metrazol is performed on epileptic patients essentially with 3 purposes: (1) for clinical diagnosis, based on the pre-

sumption that the amount of Metrazol necessary to provoke seizures is smaller in the epileptics; (2) for electroencephalographic diagnosis; Metrazol is given to provoke EEG paroxysms; (3) for the study of clinical seizures and the study of the clinical-electroencephalographic correlation in the epileptic patients. These last two purposes have different techniques and must not be mistaken one for the other.

The best technique for the EEG diagnosis in the adult over 20 years is the continuous administration of Metrazol up to 400-500 mg. diluted in 20 ml of saline solution, at the rate of 40-50 mg. per min., until EEG alterations appear. This technique induces EEG paroxysms in 80 per cent and provokes clinical seizures in 11 per cent of the epileptic patients. This method which activates only 1 per cent of the controls has a qualitative value in comparison to other techniques which only give quantitative data of a difficult interpretation. It is necessary to bear in mind the total doses as well as the speed of the injection. Both could give false interpretations.

The activation is considered positive when spikes or sharp waves appear, with or without slow waves. Clinical and experimental data support the findings that Metrazol specifically activates the cortical epileptic focus as well as the subcortical ones, though with large doses all the nervous system can be nonspecifically activated.

Metrazol activation is a useful and simple method in the adult. Results are not so evident in children and young patients because of their higher sensitivity. Other drugs have not been more useful. Sleep is an excellent method in children. Metrazol and sleep are not opposed techniques. It is necessary to exhaust all methods of activation when there is a suspicion of epilepsy.

44. Breves consideraciones sobre el EEG en el Perú y sobre algunos métodos de activación del electroencefalograma. — ALEJANDRO P. ARELLANO, Lima, Perú.

Es una presentacion preliminar con la cual se intenta iniciar una codificación de las principales características del electroencefalograma normal en los peruanos y la interpretación dinámica o psiconeurofisiológica de los potenciales eléctricos cerebrales. Se ha tenido en cuenta que el Perú es un pais geográficamente caracterizado por sus grandes extensiones andinas situadas sobre una altura de 3.000 metros sobre el nivel del mar y pobladas; por otra parte, sus habitantes son en su mayoría mestizos de indio o indígenas puros que llevan un ancestro, digamos ''incaico'', muy interesante a considerar en las implicaciones no solamente biológicas sino psicológicas en la evolución etnológica. De esto resultaría que las características psicosomáticas del peruano son un tanto peculiares dentro del complejo cultural denominado latinoamericano o hispanoamericano. En el presente estudio electroencefalográfico se hace referencia únicamente a los potenciales occipitales y frontocentrales. Se ha seguido un plan de trabajo similar al de la escuela de Boston aunque con pequeñas modificaciones.

En la segunda parte de esta presentacion se hace una breve crítica a los métodos de activacion, y se llama la atencion sobre la posibilidad de ensayar otros basados en el uso de substancias riboflavínicas o acridínicas asociadas o no a la estimulación luminosa intermitente.

45. Some comparative results of activation methods in electroencephalography. — P. PINTO PUPO and E. ZUKERMAN, Sao Paulo, Brazil.

Different methods of EEG activation, using physical or chemical stimulants, have been widely studied in the medical literature. In the majority of these studies the results are considered for each individual method. Therefore, the results obtained with one method cannot be used for comparison with those obtained with another, since the clinical material on which these different methods were studied is not identical. The authors therefore studied the effect of different methods in a single group of clinically diagnosed epileptics. In these patients the routine EEG was obtained by using the Grass 8-channel apparatus, 16 electrodes in the standard positions and the records were taken using the monopolar and bipolar techniques. Activation with hyperpnoea, sleep and intravenous Metrazol was used. In several cases, the EEG examination was repeated on another day to confirm the first results.

Studies were made on 665 patients, using routine EEG techniques, and hyperventilation performed during 3 min. From these patients, 315 were activated by Metrazol (50 mg./cc. solution, injected every 30 sec., with maximal doses of 500 mg.) and 275 patients were activated with barbiturate sleep. In 100 patients all methods were used.

The results obtained were classified as: *a*) definite paroxysmal changes; *b*) dubious changes, and *c*) no paroxysmal changes. The results were statistically studied in each group. The EEG in awake and quiet patients, without activation, showed positive results in only 29.17 per cent of the 665 cases, and, were negative in 70.80. With hyperventilation 67.90 per cent of positive results were obtained, with only 29.70 per cent negative and 4.4 per cent dubious results. With barbiturate sleep the results were positive in 37.80 per cent and negative in 62.10 per cent. Using Metrazol the results were positive in 75.75 per cent, negative in 12.4 per cent and dubious in 3.6 per cent. Considering all methods applied to the 665 cases, it appears that positive results were obtained in 78.30 per cent, negative results in 17.70 per cent and dubious results in 3.90 per cent.

The cases in which one of the activation methods did not show good results were comparatively studied with the other methods. From this study it appears that Metrazol activation was the method which showed the best results in cases in which hyperventilation and sleep were ineffective. Sleep seems to be the least effective of the activation methods.

Analyzing the cases with positive results, the authors conclude that with hyperventilation it was possible to produce positive results in the majority of patients with signs of disturbances of diffuse projection mechanisms probably due to organic lesions and also was effective in cases with focal lesions. Metrazol was of particular value in focal lesions and barbiturate sleep was the most helpful method in cases of focal lesion in the temporal lobes.

The topographical correlation of these focal cases with patients presenting bilateral synchronous dysrythmias (endogenous epilepsy ?) was also studied with these different activating methods.

46. Critical review of the various types of EEG activation, especially in children. — P. KELLAWAY.

47. Correlación electroclínica en los hematomas yuxtadurales. — C. Villavicencio y A. L. Bustamante, Santiago, Chile.

Se revisa un material compuesto por 100 pacientes con hematomas yuxtadurales comprobados. Con este material se investiga la relación entre los diversos tipos de actividad anormal que se encuentra en los EEG, con los datos y signos clínicos que se obtienen en observaciones clínicas estandardizadas con este objeto.

Las conclusiones demuestran que es posible obtener este tipo de correlación.

48. El EEG en las hernias del hipocampo. — E. Bancalari y F. Cabieses.

49. Resultados de la corticografia en pacientes hemisferectomizados y en animales decorticados. — J. A. Ghersi, A. Costales y N. Piacquadio.

50. EEG in cranio-cerebral trauma. — L. Pérez-Achard and Garcia-Austt, Montevideo, Uruguay.

The EEG records were studied of 270 patients with cranio-cerebral trauma of variable intensity. The alterations due to organic lesion were described; sixty-six per cent were diffuse. The various degrees of lesional alterations were correlated to the age, trauma, intensity and consciousness.

The epileptic discharges were very frequent and 39 per cent of them were bilateral and synchronous. The EEG disturbances in the extradural, subdural and intracerebral hematomas were studied. In mild traumas and in post-traumatic sequelae a normal EEG was found.

The value of the EEG in the diagnosis, prognosis and in the medicolegal field was studied.

51. Development of the electroretinogram in the chick embryo. — M. A. Patetta Queirolo and E. Garcia-Austt, Montevideo, Uruguay.

The ERG appears in the chick embryo at the age of 18 days of incubation showing at the same time the first evidences of the visual function. At the first stage of its development the ERG can only be obtained with a strong light adaptation and an iterative stimulation (''embryonic'' ERG type). Afterwards it acquires similar characteristics to the postnatal ERG (''postnatal'' ERG type).

The embryonic ERG has larger duration and less amplitude than the adult one. The considerable duration of the ''a'' wave is the outstanding characteristic. The retina of the ''embryonary'' type does not respond to flashes of light wave length shorter than 0.51 microns.

52. Post-tetanic fatigue and response of the superior cervical sympathetic ganglion of the cat. — V. González Panizza and J. V. Luco, Montevideo, Uruguay.

The purpose of this study is to find a technique to enable us to establish standard curves of post-tetanic fatigue and response, with the object of ascertaining the eventual changes which take place in different circumstances. The fatigue curves were obtained from statistics, the mean frequencies of supramaximal stimulation being shown by the ordinates and the duration of the stimulation by the abscissas. Each curve represents a given degree of fatigue which is defined by the negative increment of the potential in relation to the value of the normal mean. The form of the curves is similar in all cases and the frequency is a decreasing non-linear time function. The standard deviation of the mean is in general less than $\pm$ 10 per cent. The curves showing post-tetanic response were obtained by representing the mean increment of post-tetanic potential, obtained by isolated supramaximal stimulation, in the ordinates and the interval of time which follows the termination of the tetanic stimulation is given in the abscissas. The standard deviation of the means increments is in general less than $\pm$ 5 per cent. The previous tetanus provoking stimulation was supramaximal, of 10 sec. duration and a frequency of 30/sec. The maximum facilitation occurs before the first 2.5 sec. and decreases non-lineally until it becomes established after 35 sec.

The marked differences between the different cases called for a statistical study of the measurements obtained so as to make up post-tetanic fatigue and response curves. In principle their usefulness may be accepted, whilst further identical investigations are carried out in another series of animals so as to establish significant differences in the curves of the mean values, when the animals are treated in a given way.

53. Carotid sinus and EEG. — H. Mazzella, E. Garcia-Austt and R. Garcia-Mullin, Montevideo, Uruguay.

The effect of stimulation of the carotid sinus presso-receptors upon the EEG was studied in dogs. Some of these animals were awake, others were curarized and under slight barbituric anesthesia. Stimulation was effected by unilateral or bilateral distension of the carotid sinus isolated and *in situ*, by means of an intracarotid balloon or by the injection of Ringer's solution. The electrical activity was registered by two electrodes applied on the duramater in homologous regions of both hemispheres.

The sinusal distension produced, in non-constant form, a moderate slowing down of the EEG.

When one sinus alone was distended the effect was exclusively or predominantly unilateral. The action on the EEG was independent of the modifications of the arterial pressure. Intravenous injection of the ganglionic blocking hexamethonium (1 mg/kg.) did not supress the effect of sinusal dilation on the EEG.

These results are only partially in agreement with those of other authors.

54. Seno carotideo y EEG. — L. Levit.

55. Epileptic activity by cortical isolation in cats and dogs. — E. F. Migliaro, E. Garcia-Austt and J. P. Segundo, Montevideo, Uruguay.

A study was made of the electrical activity in the isolated cortex immediately following section. Cats and dogs were used. In cats the anterior part of a hemisphere was severed in a rostral and dorsal plane with respect to the thalamus. In dogs a small part of cortex was aseptically isolated (3 to 5 cm^2) by cutting its trans and subcortical connections.

It was made clear that suppression-bursts described by some authors were followed by ''spontaneous'' spikes. These last mentioned were evident in the isolated cortex of cats a few minutes after section. In dogs the same phenomenon was noticeable in 2-6

days after isolation. Spikes were more numerous in the zones lying more distant to the line of section. The slow injection of Metrazol produces the specific activation of the isolated cortex. The tonic-clonic discharge induced by Metrazol had a faster frequency and the tonic phase was longer than at the homologous area.

56. Function of the capsule of the Pacinian corpuscles. — R. Alvarez Buylla and E. F. Migliaro, México, D.F.

With the purpose of studying the part played by the capsule of the Pacinian corpuscles in their electric response to mechanical stimulation, experiments were made with corpuscles and their isolated fibers of the mesentery and mesosigma of the cat. The receptors were mechanically stimulated and their activity or that of the axon recorded by monopolar methods. It was established that the threshold and latency to the mechanical stimulation decreased when the corpuscle was subjected to a constant pressure. In this case the degree of local response necessary to start the propagated impulse was much less than if the receptor were free from all pressure. With electrodes inserted to different depths in the corpuscles no electrical phenomenon was recorded which could be attributed to capsular envelopment. When the greater part of the capsule was eliminated the corpuscle continued to respond to mechanical stimulation, but the threshold increased considerably until it was equal to that of the regenerated free terminations after the extirpation of the receptor. During the refractory period of intracorpuscular axon, the electrical responses of the corpuscle decreased until they disappeared altogether. In receptors denervated 3 weeks beforehand no electrical activity in response to the mechanical stimulation was recorded. These results would confirm that the capsule acts as a mechanical amplifier.

57. Action potentials of the sciatic nerve in the growing chick. — E. Garcia-Austt, M. A. Patetta-Queirolo and J. V. Luco.

The sciatic nerve of the chick embryo is excitable at the age of 10 days of incubation, that is to say, long before the myelinization starts. The spike potential is multiple up to the 17 days of incubation. The duration, amplitude and latency increase with the development of the embryo and chick. The conduction velocity is very slow in the embryo, less than 1 metre per sec., and does not show significant variations. After hatching it sharply increases up to 50 metres per sec. at the age of 12 days. The developing nerve shows the fatigue phenomenon entirely similar to the synaptic fatigue.

58. Estudio experimental sobre la embolia cerebral y la acción de los vasodilatadores. — V. Soriano.

EASTERN ASSOCIATION OF ELECTROENCEPHALOGRAPHERS AND SOUTHERN EEG SOCIETY

National Institutes of Health, Bethesda, Md.
and Skyland, Skyline Drive, Va.

September 30 - October 2, 1955

Secretary-Treasurer: CURTIS MARSHALL
The Johns Hopkins Hospital, Baltimore

1. Sleep as a general activation procedure. — Daniel Silverman, Philadelphia, Pa.

Whenever possible, natural or sedative induced sleep records were obtained on 1,000 consecutive patients undergoing electroencephalographic examinations at the Graduate Hospital. One-fifth of the sleep records showed variant patterns that were useful in electroencephalographic interpretation. These patterns will be described and discussed in their relationship principally to the EEG classification and clinical diagnosis. As anticipated, sleep yielded the most information in epileptics; 41 per cent had diagnostically helpful dysrhythmic sleep records. Sleep was also a valuable activation in post-traumatic states, but of less definite usefulness in other organic brain diseases.

2. Recruiting response in cortical and subcortical structures. — C. Ajmone-Marsan, Bethesda, Md.

In a series of experiments carried out (in nembutalized cats) to further investigate the functional behavior of the non-specific thalamic system it was found that very often the recruiting response not only consists of a series of potentials waxing and waning in their amplitude but these potentials also show a rhythmical variation in latency which undergoes substantial changes in value when measured in the ''waxing'' or in the ''waning'' phase. At times there is a definite relation between increasing in amplitude and shortening of the latency while at other times, the latency tends to become progressively longer only in the waning phase while remaining relatively short at the beginning of the recruiting when the amplitude of the response is not yet fully developed. It is postulated that the recruiting phenomenon may occur following excitation of shorter or longer pathways. The longest paths (those with a larger number of synapses) can be supposed to have a more restricted field of distribution but to be very effective within this limited field. Shorter paths may excite a larger number of cells but in order to do this they require considerable temporal summation. The ''recruiting'' would, therefore, depend upon a progressive activation of two main groups of elements differing from each other by the number of synapses involved and the ''waning'' phase could be due to dropping out of the neurons excited by the shortest paths.

When recording the non-specific response from a surface-cortical electrode and from a needle electrode placed at different levels within the cortex itself, the underlying white matter, radiations, various basal

ganglia and eventually the thalamus, not only the latency tends to remain the same, but recruiting and waxing and waning do occur in structures where obviously no cortical neurons are involved, and also after these have been depressed (cortical cocainization) or eliminated (cortical ablation). It logically follows that all of these events must originate subcortically and probably within the thalamus itself.

The transformation of polarity undergone by the response in the depth, its relatively unchanged amplitude and some of the mentioned observations can be explained by postulating the presence of two interrelated but separated electrical fields, one originating from fibers (positive deflection) the second from cell activity, a situation somewhat similar to that visualized by Grey Walter (1953). Thus, the transition from a high amplitude negative, to a lower amplitude negative-positive, to a high amplitude positive deflection throughout the cortex and underlying white matter can be interpreted as the result of the algebraic sum of two waves of opposite polarity with predominance of either one above or below a certain level; this level would not signify the passage from ''sink'' to ''source'' but the borderline between the two fields.

3. The effect of recruiting responses on evoked cortical neuronal discharges. — CHO-LUH LI, Bethesda, Md.

Cortical units recorded with a glass pipette microelectrode have selective properties in response to stimulation of the sensory relay nucleus and of the so-called unspecific nucleus of the thalamus. Thus, those units which discharged in response to stimulation of the nucleus ventralis posterior could not be activated by stimulation of the nucleus centrum medianum. Similarly, units which were activated by stimulation of the nucleus centromedian could not be evoked by stimulation of the nucleus ventralis posterior. However, the evoked cortical neuronal discharges were found to be invariably facilitated by the preceding volleys initiated in the nucleus centrum medianum. Similarly, units which were activated by thalamic nucleus on the activity of the cortical — sensori-neurones may have psychological implications. It is common knowledge that when an individual is ''prepared'', his reaction to a given stimulus will be influenced. These observations would suggest the physiological mechanism of ''awareness'' or ''preparedness'' to be at least partially in the unspecific thalamo-cortical system.

4. A new approach to the theory and automatic analysis of the electroencephalogram. — N. R. BURCH, A. J. SILVERMAN and T. H. GREINER, Wright-Patterson Air Force Base, Ohio.

The well known difficulties of any form of EEG analysis, treating the recording as a periodic phenomenon, will be discussed as will the inherent disadvantages in present instrumentation.

Individual EEG half-waves may be regarded as probability distributions (i.e. amplitude is considered as a function of the density of cortical events at a given instant). Some neurophysiological justification for this concept, as discussed by Rosenblith, Eccles, and others, will be presented.

This hypothesis requires treatment of the EEG as an aperiodic phenomenon, a series of ''probability waves'', best described by statistical characterization such as moments and the Gram-Charlier series, rather than by Fourier series.

A brief description of the circuits devised for automatic period analysis of the EEG will be presented, together with the type of information coding. This employs base-line cross of the primary trace to give period information and base-line crosses of successive derivatives to give wave-shape. (Illustrated with slides.)

5. Clinical and experimental application of a new method of automatic analysis of the electroencephalogram. — A. J. SILVERMAN, N. R. BURCH and T. H. GREINER, Wright-Patterson Air Force Base, Ohio.

The recording technique and play-back systems utilizing frequency modulation and magnetic tape in automatic period EEG analysis will be described. The use of magnetic tape recording presents the possibility of unlimited accurate replay, permanent easy storage, and the possibility of telemetering the contained information to a distant station.

Several clinical and experimental records will be presented and conventional methods of interpretation will be compared with automatic period analysis.

This method of automatic analysis of the EEG carries an increased amount of information, is not as inaccurate as current methods, may be used in artifact-laden situations such as field conditions. These criteria result in its applicability to the study of subtle changes — such as minimal changes in the state of consciousness.

The increased amount of information obtained in addition is available for feeding into computers for further automatic interpretation of data. (Illustrated with slides.)

6. Observations on the electrical activity of rolandic cortex in monkey. — LAWRENCE KRUGER and CHARLES HENRY, Hartford, Conn.

Electrocorticograms were obtained via implanted plate electrodes in 6 monkeys. Six point leads with 2 or 5 mm. separation between points were so placed as to record pre- and post-central activity. The animals were studied with and without anesthesia and during varying conditions of stimulation for periods up to 3 months.

Passive limb manipulation or spontaneous movement was accompanied by an alteration in the electrical activity of the contralateral cortex. This usually occurred simultaneously with or very shortly following leg movement as indicated by electromyographic recording. The change in cortical activity consisted of an increase in rhythmic fast (50-80/sec.) activity, and a reduction of non-rhythmic slower activity. The effect was seen maximally on the rostral side of the central sulcus but was recorded from electrodes at all points. It was not detectable in scalp recordings. With electrodes in the Rolandic leg area no responses were noted with manipulations of the arm or ipsilateral leg. Tactile evoked responses were limited to the contralateral post-central gyrus; no precentral or ipsilateral responses were seen. Administration of barbiturate enhanced the fast activity response to movement and tactile evoked responses, but Dial tended to obscure the precise somatotopic distribution of tactile responses.

In one animal the lead was placed over precentral cortex, at the time alumina cream was injected into the cortex, to follow the subsequent development of seizure activity. This preparation also showed some alteration of spontaneous activity with movement,

but the early onset of seizure discharges soon masked the effect.

7. Quantitative studies of slow wave activity following electroshock. — MAX FINK and ROBERT L. KAHN, Glen Oaks, N.Y.

In the course of an investigation of altered brain function following electroshock, various measures of slow wave activity were correlated with alteration in behavior. Electroencephalograms were done on 24 consecutive patients referred for electroshock therapy. Records were taken prior to and at weekly intervals during and following the course of treatment. The total of 160 records so obtained were classified according to five criteria: the average per-cent time slow waves (7 c/sec. or less) for three given lead combinations (frontal-parietal, anterior temporal-vertex, and parietal-ear lobe), the highest per cent time slow wave in any one lead combination, the lowest slow wave frequency, the duration of the longest bursts and the highest slow wave amplitude. On the basis of percentile scores obtained for each factor, the relative position of each record was determined. Those in the upper third of the distribution were considered to have high degree abnormality, while those in the lower third were low degree abnormality. Ratings of degree of alteration in behavior were made by the supervising psychiatrist and the patients were characterized as "much improved", "improved", and "unimproved".

The following correlations were significant:

(1) A positive correlation between degree of alteration in behavior and degree of EEG abnormality was demonstrated. Of the much improved patients, 25 per cent showed high degree EEG abnormality after one week of treatment, 80 per cent after two weeks and over 90 per cent after three weeks. In the unimproved patients, however, none had a high degree abnormality record during the first three weeks and only one had such a record by the fourth week of treatment.

(2) Analyzing the relation of altered behavior to each of the measures of slow wave activity, demonstrates a positive correlation for each index.

(3) Each of the indices of slow wave activity were significantly correlated with each other.

The significance of these observations for electroshock therapy, and the validity of these indices in electroshock studies will be demonstrated.

8. A neurophysiological test which differentiates between neurotic and psychotic depression. — CHARLES SHAGASS, Montreal, Canada.

It is often difficult to distinguish between neurotic and psychotic depressive states. This study was carried out to determine whether an objective test, the sedation threshold, would facilitate this differentiation. The sedation threshold is the amount of sodium amytal, required to produce certain quantitative changes in 15 to 30c/sec. activity of the frontal EEG; these changes usually accompany slurred speech (Shagass, C. *EEG Clin. Neurophysiol.*, **1954**, *6*: 221-233).

Of 440 consecutive patients tested, 182 were selected for study. This included all patients classed: psychotic depression, schizo-affective psychosis (depressed), "hysterical" depression, neurotic depression and anxiety state. Mean thresholds, in mgm./kg., were: psychotic depression, 2.82; schizo-affective, 2.86; "hysterical" depression, 2.70; neurotic depression, 5.05; anxiety state, 5.32. The sedation threshold achieved a 95 per cent differentiation between the psychotic and neurotic depression groups. Short-term response to electroconvulsive therapy (ECT) was superior in patients with low sedation thresholds than in patients with high thresholds. Patients tested after recent ECT had significantly higher thresholds.

Results indicate that the sedation threshold can be used as a practical differential diagnostic test in depression. Relation of the findings to theories of anxiety and depression will be discussed.

9. Differences in the per cent alpha time between male and female alcoholics. — ALBERT N. BROWNE-MAYERS, New York, N.Y.

This paper is a very brief survey of a series of over 100 male and female alcoholic patients (about equally divided) who were admitted to Payne Whitney Clinic during the past 4 to 5 years. In this particular group the female alcoholics showed a preponderance of per cent time alpha activity below 40, whereas the per cent alpha time of the male alcoholics were above 50. A comparison of these findings with other clinics will be discussed.

10. The use of an FM tape recorder for pen and ink recording of fast EEG and EMG frequency components. — W. T. LIBERSON and ROBERT W. SMITH, Northampton, Mass.

11. Electric activity of the olfactory bulb in man. — CARL. W. SEM-JACOBSEN, MAGNUS C. PETERSEN, HENRY W. DODGE, Jr., QUENTIN D. JACKS, JORGE A. LAZERTE and COLIN B. HOLMAN, Rochester, Minn.

The electric activity of the olfactory bulb has been studied in 17 patients. Recordings were made from 21 implanted microelectrodes. Electrodes were placed in both bulbs in two patients, while two electrodes were placed in the same bulb in two patients.

Stimulation of the nasal mucosa by odor evoked electric rhythms from the olfactory bulb varying from 26 to 39 c/sec. The previously indicated existence of a spectrum of electric frequency in the bulb induced by odors is given some further support. Electric rhythms elicited by odor were not synchronous, either in both bulbs or in different parts of the same bulb. The responses recorded from an individual electrode were maximal with only a limited number of odors. The response to the same odor recorded from various electrodes ranged from none to maximal. Likewise, the response to various odors recorded from the same electrode varied from none to maximal.

It is extremely unlikely that all electrodes were in the same minute anatomic region of the bulb. Thus, the findings may indicate an anatomic distribution of regions in the bulb giving maximal response to a small number of odors or components of odors only.

These findings may be of value in solving the problem of discrimination of smell.

12. Bioelectric potentials of the alligator mississipiensis. — WALTER D. OBRIST and KAO LIANG CHOW, Hartford, Conn. and Chicago, Ill.

The electroencephalogram, electrocardiogram and respiration muscle potentials of four alligators were recorded from stainless steel needle electrodes on standard EEG equipment. The alligators varied in age and size; the smallest was 30 inches in length; the largest, 74 inches.

Electrical recordings from the surface of the head revealed semirhythmic 4-7/sec. activity over the brain stem and cerebral hemispheres, with the greatest amplitude over the brain stem. When the alligators were turned on their back, a state of tonic immobility was induced that was accompanied by a marked reduction in voltage of the EEG. A decrease in the EEG frequency was observed during periods of apnea and slow heart rate. An increase in frequency followed auditory and tactile stimulation.

The electrocardiogram showed a ventricular rate of 25 to 30 per minute. A slowing of the heart occurred following auditory and tactile stimulation, in some instances to as low as 4 systoles per minute.

Respiration rate was highly variable, averaging 5 to 7 per minute. Auditory and tactile stimulation resulted in periods of apnea ranging up to 8 min.

The authors are indebted to Dr. Perry A. Sperber of the Sea Zoo, Daytona Beach, Florida, for supplying the alligators.

13. Special clinical and EEG problems of patients with seizures in a large mental hospital. — HENRIETTE L. WAYNE and JOHN L. HASKINS, Los Angeles, Calif.

A review of the hospital population with convulsive seizures in a large mental hospital elicited certain diagnostic and therapeutic differences in comparison with those usually encountered in seizure clinics or in practice. Not only were all patients chronically ill mentally, and most of them psychotic, but a surprisingly large number were not primarily epileptics and had originally suffered from other forms of neuropsychiatric diseases.

Approximately sixty patients were schizophrenics (paranoid, — hebephrenic, — catatonic, — undifferentiated, types) and had developed convulsive seizures only after exposure to shock therapy. A small number of post-lobotomy cases will be discussed in comparison. The clinical and EEG problems connected with the schizophrenic groups, in particular their relationships to age, duration of illness, number of shock treatments, and possible precipitating factors will be discussed.

14. The use of histamine as an activating adjuvant in EEG. — L. LAPINSOHN, Philadelphia, Pa.

The use of histamine as an activating adjuvant in EEG has never been reported in the literature. Its use in the EEG study of a case clinically diagnosed as Horton's histamine cephalagia is presented. The correlation between the EEG record and concomitant clinical symptoms, along with the subsequent clinical course of the patient are discussed. The neurophysiologic and neuropharmacologic implications of these findings are elaborated upon in the light of the observations previously presented.

15. Asymmetrical EEG foci in cerebral palsy. — JAMES W. WARD, Nashville, Tenn.

This study is based on the EEGs of patients with cerebral palsy. Of 75 patients having a clinical diagnosis of cerebral palsy 17 had one or more episodal records showing among other things multiple foci made up chiefly of slow spikes or slow spike variants. Between these foci the slow spikes exhibited phase reversal during unipolar recording. No consistent correlation could be made between the foci with positive or negative take-off with respect to a given patient's symptoms. There was no clear difference in symptoms between these patients and the others who showed other types of abnormality in their EEGs. Evidence that the foci exhibiting phase reversal may have a common deep origin is considered.

16. Effects of sodium diphenyl hydantoinate (Dilantin) upon the isolated rabbit small intestine. — FLOY J. MOORE and RALPH DRUCKMAN, Houston, Texas.

A concentration of 1 mgm. per cent of sodium diphenylhydantoinate was effective in reducing the amplitude of contraction of the isolated rabbit small intestine. Concentrations of 8 mgm. per cent abolished recordable contractions.

It has been reported that the blood levels of hydantoinate in human patients receiving sodium diphenylhydantoinate for the treatment of epilepsy ranges between 3 and 6 per cent. Thus, it is obvious that the range of concentrations of sodium diphenylhydantoinate employed in these experiments were well within the therapeutic range. This is of some practical significance, as these findings may help to explain the constipation which sometimes develops in patients taking diphenylhydantoin (Dilantin).

These results may also be of importance in relation to the problem of so-called ''abdominal'' epilepsy. Commonly accepted criteria for the diagnosis of this form of seizure include (1) episodic attacks of abdominal pain, (2) ''cerebral dysrhythmia'' as revealed by electroencephalography, and (3) improvement with marked reduction or cessation of these attacks upon the institution of anti-epileptic medication, usually with diphenylhydantoin sodium. The implication has been that improvement upon the institution of this medication is due to an effect upon the central nervous system. The possibility of such improvement being due to a direct effect of the medication upon the gut has not been given adequate consideration. If, as has been demonstrated in these experiments, the diphenylhydantoin sodium has a direct effect upon the gut, then the third criterion is no longer necessarily valid in indicating the ''central'' origin of these attacks. The problem of ''abdominal'' epilepsy should be considered without regard for the effects of anticonvulsant medication, unless the direct effect of this medication upon the gut can be dissociated from its effects upon the central nervous system.

The rapid reversibility of the effects of diphenylhydantoin upon merely replacing the solution of diphenylhydantoin sodium with fresh Tyrode solution probably indicates that the drug does not form any strongly bound compound in the isolated gut and also indicates the essential harmlessness of this agent. Whether the diphenylhydantoin sodium acts by a direct effect upon the smooth muscle cells or by an effect upon the nerve plexuses in the wall of the gut is unanswered in the present experiments.

17. Early and late seizures after closed head injury with serial electroencephalographic observations. — JOHN T. MANTER, Augusta, Ga.

Among 405 patients (aged 14 months to 61 years) with mild or moderate closed head injury, excluding birth trauma and subdural hematoma, 131 had abnormal electroencephalograms. Seven of these have had seizures which were considered to be directly related to trauma. Serial electroencephalograms were obtained in 5 such cases.

Immediate focal convulsion after mild trauma was associated with localized slow waves in two of three patients — all of them children. (Initial and repeated electroencephalograms of the third child were considered normal.) Abnormal slowing disappeared within a few weeks and seizures have not recurred in this group.

Seizures developing 6 months to 2 years after trauma have a dissimilar pathogenesis. Serial electroencephalograms in these cases have shown moderate diffuse abnormalities persisting for 6 months or more before slow improvement was apparent. A slow wave focus may, or may not be demonstrable at some interval of the recovery period. After normal, or near normal patterns were reestablished, paroxysmal abnormality appeared abruptly and preceded the onset of generalized seizures.

Prolonged time lag in the dissipation of electroencephalographic abnormality after trauma is considered to be more significant than the degree of disturbance in any single record, and is possibly an indication of contusion. Electroencephalographic observation should continue for two years to disclose evidence of posttraumatic epilepsy.

18. Electroencephalographic activation with scopolamine and alpha chloralose. — Russell R. Monroe, Robert G. Heath, William Miller and Charles Fontana, New Orleans, Louisiana.

Alpha chloralose, used clinically as a sedative, has been rarely but quite successfully used as an electroencephalographic activator in epileptics. It was reported that in certain individuals activation released psychotic-like behavior which was not typical of the usual psychomotor attack. This study reports on activation in 37 hospitalized patients with psychotic behavior, and 15 normal controls. Eight of the psychotic patients had intracranially implanted electrodes.

Only 3 of the 37 hospitalized psychiatric patients failed to show activation after receiving orally 500 mg. of alpha chloralose and 1/2 mg. of scopolamine. This activation occurred despite the fact that only 7 in this group showed some irregularities in their baseline electroencephalogram, and only 7 had a history of even isolated clinical seizures.

In the 15 control subjects, 4 were activated. These 4 showed minimal build-up during baseline hyperventilation.

Activation occurred within the first hour and reached a maximum within the second. There appeared a gradual slowing of the record, often focal but usually becoming generalized later, with a maximal effect of paroxysmal high amplitude hypersynchronous activity. Occasionally sharp waves or spikes (focal) were noted. In those patients with subcortically implanted electrodes, there was no conclusive evidence of subcortical involvement preceding cortical activation.

All the patients who showed paroxysmal activation demonstrated dramatic clinical changes in behavior, but only one lost consciousness. The behavioral changes were usually similar to the psychiatric symptomatology and not necessarily associated with clouding of sensorium.

19. Histamin and antihistamin activation of the electroencephalogram. — George D. Gammon and Melvin Thorner, Philadelphia, Penna.

Gammon *et al.* have previously reported on the use of antihistamines, particularly pyribenzamine and Benadryl, in studies on epilepsy. Both these substances were found to activate both the EEG dysrhythmias and the convulsive syndromes in epileptics. Of particular value was the use of these two substances in activating the normal control EEG of known epileptics. In this circumstance, a high percentage of true diagnostic positive records could be produced with few false negatives. In non-epileptic subjects such activation produced very few false positives.

As an extension of this study (after Lapinsohn and others) intravenous histamin was tried as a possible activator. Preliminary studies show that, in the same group of subjects, histamin, given to the point of beginning vasomotor signs and headache, produced similar results. From our data so far this activating action is well established.

This apparent paradox is susceptible of several possible explanations. (1) the two antihistamines used act by virtue of some property other than blocking histamin. (2) In pharmacology it has been sometimes observed that an agonist and antagonist may have the same *immediate* effects. The time intervals in our study do not favor this hypothesis. (3) Either substance may disturb cerebral homeostasis so that dysrhythmia results in epileptic subjects. This latter kind of reasoning is not readily reducible to experimental proof.

Finally, we believe these three substances should be used only with caution among epileptics.

20. An informal symposium was also held on *Problems of Interpretation of the Normal EEG.* — J. K. Merlis and P. Kellaway were Moderators. The panel consisted of W. T. Liberson, S. Little and R. S. Schwab.

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THE EEG SOCIETY

October 15, 1955, at the National Hospital,

Queen Square, London, W.C. 1

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1. A verified case of secondary bilateral synchrony. — J. A. V. Bates, W. Cobb and D. J. Wiliams, National Hospital, Queen Sq., London.

A case was described of a child of 12 with a severe aggressive behaviour disorder and grand mal attacks in whom surgical removal of diseased brain appears to have produced a sudden and complete cure (9 months). A lesion was not suspected as a result of clinical examination, air-encephalography or arteriography but the EEG showed frequent bilateral frontal sharp and slow wave complexes. Secondary bilateral synchrony was suspected from slight but consistent differences on the two sides, and an area of electrical dysfunction in the left frontal lobe was confirmed by the absence there of a barbiturate fast response. A left frontal flap was turned on EEG evidence alone and a large angiomatous malformation with evidence of old haemorrhage and thrombosis was revealed. In this case we were fortunate in having an EEG record of five years previously which showed a left fronto-temporal slow wave focus. The lesion which had caused the pathological aggression was entirely frontal.

2. The recurrent syndrome in children : clinical and electroencephalographic observations in 52 cases. — R. C. Mac Keith and G. Pampiglione, Guy's Hospital, London.

It has been suggested that recurrent abdominal pain and "cyclic vomiting" are related to epilepsy. The argument is usually based on EEG findings described as abnormal and the beneficient effect of anticonvulsant drugs. The reported cases are single or in short series; the EEG findings have not always been judged by recent standards and they are widely varied; the drugs used were often sedative as well as anticonvulsant.

The present series describes findings in 52 children aged 3 to 15 years, average age 9 years, who came with recurrent headache, vomiting, abdominal pain or pyrexia — the four symptoms commonly seen alone or together in the recurrent syndrome. The children were originally seen in Out-Patient departments by a paediatrician (R.C.M.) or, in a minority of cases, by a colleague in the same clinic. Children with local causes of their symptoms were excluded. Electroencephalography was originally used in these cases as an aid to the exclusion of gross intracranial disease and not with the intention of finding whether the recurrent syndrome itself has special EEG features. Only 6 of the children had more than one EEG taken. As this present retrospective study is to find whether there are special EEG features in the recurrent syndrome, children with a history of convulsions, concussion or neurological disorder which might have caused EEG abnormalities are considered separately. The EEGs which had originally been reported on by various persons were re-examined by one person (G.P.) over a short period of a few days so that criteria of normality would be fairly uniform.

Four children were examined by EEG *during* one of their recurrent episodes of abdominal pain or headache, one being re-examined when feeling well. Of these four, one had a record normal throughout; one had a borderline record; one a mildly abnormal record (mild asymmetry of alpha rhythms in amplitude and frequency, few sharp elements and a probable excess of 4-7 c/sec. activity, for a 12 year old boy, before the beginning of the headache, but a much more regular appearance of the record during headache and just before vomiting); and one during an attack of pain over the left eye with flushing of the forehead had an abnormal record which showed some irregular 3-7 c/sec. activity and few sharp elements more marked over the right than over the left frontal region. In this child a second record taken under Seconal induced sleep three days later disclosed no definite abnormalities.

Of the remaining children, 12 had normal EEGs, and 25 borderline or mildly abnormal records (excess of 3-7 c/sec. activity with moderate asymmetries, posterior temporal slow or sharp waves blocked by eye opening). Eleven had definitely abnormal records (sharp waves outside the parietal temporal regions not blocked by eye opening, marked asymmetries, paroxysmal changes of various kinds to be described. Two of the children had generalised bursts of rather irregular spike and wave complexes without having subjective clinical phenomena).

Some comments about the clinical and EEG problems involved in this group of patients are offered for discussion.

3. Occipital delta rhythm in relation to centrencephalic. — Catherine Elston, N. Gordon and W. Cobb, National Hospital, Queen Square, London.

The EEGs of some patients with petit mal contain, in addition to characteristic episodes of spike and wave complexes, a 3/sec. rhythm of large amplitude in both occipitotemporal regions, very responsive to eye-opening and closing, and to overbreathing; 40 of

such patients have been compared with 40 otherwise similar, but without the occipital delta rhythm.

All the 80 patients are under 16 years of age. As a group those with delta rhythm have an earlier age of onset of their fits, fewer major attacks, many more minor attacks and rather more affected relatives. Their siblings, whether having fits or not, tend also to have occipital delta rhythm. They are strikingly more difficult to control with drugs. They correspond fairly closely with the category of Pyknolepsy and, hence, the final prognosis should be good, but of this we still have inadequate evidence.

The characteristics of the occipital delta rhythm are relatively constant and do not seem to differ significantly from similar rhythms seen in patients with lesions, except that such patients may be older. These lesions almost certainly produce their effect at the superior collicular level of the brain stem, or possibly in the posterior thalamus. It is not unprofitable, therefore, to compare these two groups of cases with occipital delta rhythm in the light of the concept of centrencephalic epilepsy.

4. Slow potential changes in epilepsy and other conditions. — W. Grey Walter, Burden Neurological Institute, Bristol.

The directly coupled transistor amplifier developed for technical experience happens to be admirably suited for studying slow changes of potential in the EEG, since it can be operated without a mains or ground connection or in parallel with conventional systems. The inherent rate of drift is less than the equivalent of 10 μV. A number of patients and normal subjects have been studied with this system. Most normal records exhibit very little in the way of slow potential changes, nor do the slow waves of infancy, overbreathing or sleep appear greatly different in the D.C. channel. On the other hand focal delta waves near cortical lesions and the wave-and-spike of petit-mal are monophasic (i.e. all above or below the base line) and negative near the focus. The field of these slow monophasic waves is often very complex and is sometimes related to the focal discharge of spikes. Moreover in certain types of epilepsy, notably the abrupt fast wave-and-spike, there is also an ''integration'' effect, seen as a very slow, steady change in P.D. during the seizure, which persists for some seconds after the end of the seizure pattern and may amount to several millivolts. The region first and principally involved in the wave and spike discharge is negative to other regions but the field of the slow change is usually complex, with several peaks and re-entrants. These monophasic and sustained potential changes seem as close to a pathognomonic feature as anything yet described in the EEG; there is a possibility that they represent the metabolic segment of a vicious circle tending to cerebral instability.

5. The EEG in 22 cases of murder or attempted murder, together with a discussion of the possible significance of alphoid rhythms. — A. C. Mundy-Castle, Johannesburg, South Africa.

A detailed study is presented of the EEGs of 15 African and 7 European persons, mostly drawn from a mental hospital, involved in 20 murder and 2 attempted murder cases. The group contained 27 per cent confirmed epileptics and 73 per cent EEGs, including 27 per cent with unilateral temporal lobe foci. Details of all abnormalities and unusual features are presented and it is concluded that in general the results support previous findings, in that EEG abnormalities may be related to diminished culpability for capital crimes. This view accords with the conclusions of the courts concerning the present series.

A number of problems are raised by the high incidence (64 per cent) of anterior alphoid rhythms found in this group. This activity has previously been reported as common among normal Africans, but the incidence among the present Africans is significantly greater than in normals. An Appendix is devoted to discussion of the possible significance of alphoid activity.

6. Some peculiarities in the response to flicker in cases of migraine. — A. L. Winter, Burden Neurological Institute, Bristol.

A chance observation during routine EEG examinations has led to the investigation of ''flicker'' responses in migraine, particularly the response to frequencies above the alpha band. An analyser has been used in all examinations and recently a ''step-time'' switch, a device for automatically controlling the duration and frequency of the stimuli has been introduced.

One hundred cases of clinically diagnosed migraine have been studied, some many times, and there is a prospect of introducing an EEG classification of migraine and other types of headaches.

The technique employed and the method of classification of the findings for diagnostic purposes will be briefly described together with a few examples.

7. The alpha rhythm and rate of visual perception. A preliminary investigation. — A. C. Mundy-Castle, Johannesburg, South Africa.

The implication by the scanning hypothesis of a relationship between perception and alpha frequency was tested by an experiment involving tachistoscopic presentation of various numbers of figures drawn on cards. Fifty-four subjects were tested, each being given an independent EEG recording for determination of alpha frequency. Two significant correlations emerged: the highest number of complex non-geometric figures accurately perceived, and the highest number accurately perceived and subsequently recognised, were both associated with alpha frequencies. No significant correlations were found between alpha frequency and number perceived of circles or letters enclosed by circles. It is concluded that these findings confirm the heuristic value of the scanning theory, and indicate a profitable field for further research.

8. Lerner's polar analyser applied to EEG. — A. M. Andrew, Massachusetts Institute of Technology and Glasgow University.

The name ''polar analyser'' has been given to a type of electrical network. It receives one input signal and gives two outputs, and has the property that if the input is sinusoidal and within a certain frequency range, the outputs are both sinusoidal and there is a phase difference between them of 90 degrees. Furthermore, the two outputs are equal in amplitude, and their amplitude is a fixed fraction of the input amplitude throughout the frequency range. Thus if the two outputs are connected respectively to the X and Y deflection amplifiers of a cathode-ray oscilloscope, the spot moves in a circle, making one revolution per cycle of the input. A polar analyser for the EEG range of frequency has been

designed by R. M. Lerner of the Research Laboratory of Electronics at M.I.T.

When unfiltered EEG waveforms were applied to the polar analyser, the resulting pattern seemed too complicated and non-repeating to be of value. The polar analyser has therefore generally been preceded by a filter selecting a fairly narrow frequency band. The spot of the cathode-ray tube then moves in a circle, making one rotation for each cycle of the rhythm selected.

The technique can be used to look for effects of the kind reported by Boreham, Kibbler and Richter and by Bates, who showed that certain movements by a subject are more likely to occur at some parts of the phase of the alpha rhythm than at others. For this application, the cathode-ray tube spot is darkened, and only brightened briefly when the subject makes the movement being considered. A photograph of the cathode-ray tube screen, taken with a long exposure time, provides a scatter diagram showing the distribution of occurrences of the movement. The variation with frequency of the phaseshift introduced by the band-pass filter can be compensated for by delaying the brightening of the spot by a fixed amount.

The method can also be used to determine whether the EEG contains a component synchronised to a stimulus, by arranging that the brightening of the spot occurs at the same time as the stimulus. The method could also be used to trigger a stimulus from the EEG in a manner similar to the method of Hewlett.

9. Some microelectrode studies of the burst response in isolated cerebral cortex. — B. Delisle Burns, B. Grafstein and J. Olszewski, Department of Physiology, McGill University and Montreal Neurological Institute, Montreal.

In neurologically isolated unanaesthetized cerebral cortex a single stimulus applied to the surface of the cortex may produce a burst of neuronal activity, which is synaptically transmitted in all directions from the stimulated point (Burns 1951). The activity causes the surface of the cortex above the active region to become positive with respect to its resting state. From the properties of this surface-positive burst response it has been possible to make certain deductions about the shape and position of the neurones which transmit the response (Burns and Grafstein 1952). The present experiments were undertaken in order to identify these neurones histologically.

A solder-filled glass microelectrode tipped with iron was slowly inserted into the cortex until it appeared that the microelectrode tip was lying close to the cell bodies of some of the neurones which participate in the burst response, since single unit potentials were recorded only during surface-positive bursts. The position of the micro-electrode tip was then marked by passing a weak current through it, thus transferring a small quantity of iron from the electrode tip to the tissue. The iron deposit was later stained and its position determined in histological sections. It was found that of 36 marks made in this way, 26 were located in layer V, while the other 10 were scattered in layers II, III, IV and VI. However, these marks indicated only the positions in which the largest single unit potentials had been obtained, and smaller unit potentials during surface-positive bursts could be recorded at any depth in the cortex between 0.2 and 1.3 mm. Since the maximum amplitude of these potentials at any point equal to or greater than the maximum amplitude of injury discharges recorded at the same point, it appears that the population of neurones which is excited during burst responses includes all the largest neurones whose cell bodies lie in layers II-V. However, the synaptic paths which link these neurones are still unknown.

References:

Burns, B. D. *J. Physiol.*, **1951**, *112*: 156.
Burns, B. D. and Grafstein, B. *J. Physiol.*, **1952**, *118*: 412.

10. A transistorised EEG amplifier. — W. Grey Walter, Burden Neurological Institute, Bristol.

During the last two years several transistor circuits have been investigated. Among these, the most promising is a straightforward balanced push-pull system which is surprisingly similar to the conventional vacuum-tube arrangement, and has comparable properties. There are three amplifying and two coupling stages, using altogether ten transistors type 3X/302 N manufactured by Standard Telephones & Cables. The input impedance is about 20 k.ohms, the voltage gain about one million, output power 500 mV. into a standard Ediswan ECG pen recorder giving 2.5 cm. peak to peak deflection with critical damping. The noise level is about 3 μV. peak to peak on short circuit.

The whole amplifier can be directly coupled or can be used with a single RC coupling. The pre amplifier (3 stages) consumes 600 μA. at 30 V., the power amplifier (2 stages), 25 mA. at 30 V., the overall efficiency (power output compared with total consumption) being about 60 per cent. The amplifier to be demonstrated has been made up with full sized components and measures 12" $\times$ 2" $\times$ 2½" including batteries; with miniature components it could easily be half this size. The total component cost (excluding pen recorder and paper drive) is £25. The effects of temperature and battery changes are automatically compensated over the normal range; there is no trace of microphony and the performance has remained constant over a period of twelve months. EEG calibration and clinical records taken with this system are indistinguishable from conventional ones. There seems no reason why a portable 6-channel instrument should not be made to fit into a brief-case at a cost of less than £500.

11. Convergence of specific and unspecific afferent impulses on neurons of the visual cortex. — O. Creutzfeldt, G. Baumgartner and R. Jung, Freiburg, Germany.

Single neurones in the visual cortex recorded extracellularly with micro-electrodes were explored using light flashes and intralaminar thalamic stimulation separately and together. Intralaminar stimulation causes a process of discharge or an inhibitory pause in many neurones which show different reactions to light. A discharge from A-neurones following intralaminar stimulation can be different in light and darkness although these neurones do not react directly to light. The neuronal discharge after intralaminar stimulation begins at the same time as the long latency surface negative response, usually 30-50 msec. after the stimulus. This is followed by a succession of group discharges associated with waves of 100-200 msec. duration. Short latency responses occurring a

few msec. after intralaminar shock can also be seen. These apparently come from very small neurones because generally they appear only as a thickening of the base line. The pattern of neuronal discharges after light flash and intralaminar shock generally shows convergence of the responses from specific and unspecific afferents. This convergence seems to work generally with algebraic summation of both excitation and inhibition, which occur after each type of stimulation separately. This is true for the primary discharge and for the following rhythmic afterdischarge. In some neurones occlusion of two separate excitatory processes in specific and unspecific afferents can be observed instead of algebraic summation. The mechanism and site of this convergence has not yet been determined, but it is probably in pre-synaptic pathways, whether intracortical or subcortical remains uncertain.

12. Inhibition at single cortical neurons after electrical stimulation of homolateral and contralateral sensori-motor cortex. — R. JUNG and O. CREUTZFELDT, Freiburg, Germany.

In the cat "encéphale isolé" preparation the cortical surface has been stimulated with square wave 1 msec. pulses and recordings have been made with extracellular electrodes (tip 1-3 μ) inserted below the surface.

Stimulation of the cortical surface causes two different processes, one of inhibition and one of facilitation of single cortical neurones. After a single stimuli an inhibitory pause of discharge of 150-400 msec. duration is constantly observed. This occurs whether or not the neurone has discharged in the first milliseconds after the stimulus. In low frequency stimulation, up to 4 per sec., this inhibition of unit discharge is the most obvious result of stimulation on the neurone, although a sharp wave of more than 20 msec. duration is observable from the cortical surface. The inhibition pause begins generally with this wave, lasts during the silent period until a rhythmic train of waves appears. During these waves the neurone is discharged again. After higher frequency stimulation, over 5 per sec., facilitation comes in with a regular discharge in the first milliseconds following the stimulus. This brings the cortex into a pre-convulsive condition. With continuous repetitive stimulation a self-sustained convulsive discharge appears. The long inhibitory pause was always found on the site of stimulation as well as on the symmetrical point of the contralateral hemisphere. The results can be explained by assuming two different processes: a slow and easily fatigued inhibitory process and a short facilitating one which is capable of summation, breaking down the normal restraining forces of cortical co-ordination.

13. Juvenile epilepsy: genetic and electroencephalographic studies. — J. D. METRAKOS, KATHERINE METRAKOS and F. C. FRASER, Montreal, Canada.

In 1952 Metrakos, Metrakos and Fraser began an investigation of the near relatives (siblings, parents, grandparents, aunts, uncles and cousins) of epileptic probands (mean age = 94.5 $\pm$ 7.2 mos.) from the Neurology Service of The Montreal Children's Hospital who have: (1) a history of recurrent petit-mal and/or grand-mal seizures; (2) no obvious neuropathology to account for their seizures; and (3) a centrencephalic type of electroencephalogram. Appreciating the difficulties but also the paramount importance of an adequate control, patients who have: (1) no history of seizures; (2) no neuropathology; and (3) a normal electroencephalogram are selected at random to form the control probands. The near relatives (5388) of 90 centrencephalic and 70 control families have been studied. Numerous comparisons suggest that the two groups of families are comparable and that there are no variable factors other than those to be studied. In the frequency of seizures and electroencephalographic abnormalities no sex difference was obtained.

A relative of the proband is classed as affected if he has a history of one or more seizures whatever the cause. It must be clearly stated, therefore, that individuals who are classed as affected cannot be regarded as belonging exclusively to the centrencephalic class. On the other hand, of all the affected relatives, approximately 88 per cent had three or more epileptic episodes and in addition many of these were on drug therapy and could be classed as chronic epileptics.

As the genetic distance between the relative studied and the proband increases, the frequency of affected individuals tends to decrease (from approximately 20 per cent in the parents and siblings to 2-3 per cent in the grandparents and cousins) in the case of the centrencephalic group, but tends to fluctuate within fairly narrow limits around 2.3 per cent for each class of relative in the control group. When all the near relatives are considered together, the frequency of affected individuals in the centrencephalic group (5.99 per cent) is approximately 2 and a half times and significantly higher ($P = < .001$) than in the control group (2.33 per cent). Since the frequency of seizures among the siblings is essentially the same whether one parent is affected or not, and since seizures tend to appear more frequently in the "affected-parent" side of the family, dominant inheritance with reduced penetrance is a likely mode of transmission, and, at the present time, the simplest explanation.

The overall prevalence of electroencephalographic abnormalities in the parents and siblings considered together is significantly higher in the centrencephalic group (36.11 per cent) than in the control group (21.51 per cent). However, with the probable exception of "centrencephalic" and "non-specific bilateral theta rhythms" types of electroencephalographic abnormalities, there is at the present time no conclusive evidence that specific types of cerebral dysrhythmias are more frequent in the centrencephalic than in the control group.

The results of these and of other investigators are in general agreement that there is a higher frequency of convulsive disorders among the near relatives of epileptics than in non-epileptics. However, there is less agreement on the etiological importance of the hereditary factors and even less agreement on the actual type of inheritance involved. The widespread existence of cerebral dysrhythmias, particularly in children, restricts the value of electroencephalography for differentiating "carriers". In view of all these difficulties and uncertainties, genetic counselling must continue to be guarded.

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902 Boren Ave. Seattle 4, Wash.

1. Photic stimulation in organic cerebral dysfunction. — K. A. Kooi, H. G. Eckman and M. H. Thomas.

This report describes characteristics of the electroencephalographic response to photic stimulation in 81 patients with organic brain damage as evidence by neurological or psychological examination, air studies, arteriography, operation or autopsy. The findings are compared with those seen in 90 control subjects. The EEG data will be presented in relation to such clinical variables as chronicity of the illness, localization of the lesion, presence or absence of convulsions or visual defects and mental state. The value of photic stimulation in the detection of organic cerebral dysfunction will be discussed.

2. Photic stimulation as an activating agent in epilepsy. — Henry S. Colony and Edmund A. Mackey, Oakland, Calif.

Photic stimulation was used as an activating agent alone in 239 cases. One hundred and one of these were cases of verified epilepsy. The remainder had other diagnoses. Nine cases of epilepsy had paroxysmal discharges with photic stimulation. Only 4 of these had previous normal tracings in unactivated tracings. Six cases with other diagnoses had paroxysmal discharges with photic stimulation. This series of cases would indicate that photic stimulation used alone as an activating agent is certainly of limited value.

3. EEG changes in convulsive states produced by ACTH. — N. A. Bercel, Beverly Hills, Calif.

Six cases of convulsions following cortico-steroid medication were described. In four, seizures were preceded by a toxic psychotic picture with paroxysmal slow wave bursts appearing from a slower than normal background. Careful elimination of electrolyte imbalance more than anticonvulsant medication terminated the seizure state. In two cases, spike and dome complexes and a family history of epilepsy was found. Here corticosteroid medication seemed to have suddenly lowered the already low convulsive threshold and evidence for electrolyte imbalance was minimal. In this group, seizures occurred after relatively small doses of ACTH.

4. Electroencephalographic findings in cerebellar tumors. A review of current and old concepts. — Robert S. Dow, Portland, Ore.

Previous concepts of the electroencephalographic changes in the posterior fossa or cerebellar tumors were reviewed. The electroencephalographic findings in 51 consecutive patients having tumors in the posterior fossa were analyzed. It was found that there was no focal abnormality characteristic of cerebellar tumors.

When focal changes were found, they were not as well defined and definite as in cerebral neoplasms. Their presence, however, does not rule out a cerebellar lesion. The concept of occipital foci being characteristic of cerebellar lesions should be discarded. Normal or borderline records do not rule out these lesions though they are more common than would appear to be the case with expanding intracranial lesions as a whole. Normal records are apt to be found in tumors in either the medulla or outside the cerebellum, or if in the cerebellum, in very young patients early in their disease.

We are inclined, on the basis of our results, to attribute the changes seen to the obstructive effects of these lesions on cerebral spinal fluid circulation with secondary internal hydrocephalus and dilation of the third ventricle, as did Daly, Whelan, Bickford and McCarthy in 1953.

5. The effect of alcohol on the electroencephalogram. — Henry W. Newman, San Francisco, Calif.

A rising concentration of alcohol in the blood of human subjects produced progressive increase in slow activity in the EEG. The concentration at which this became manifest varied from individual to individual over a wide range, but correlated fairly well with that at which clinical manifestations of intoxication were demonstrable. This constitutes definite proof that differences in individual tolerance to alcohol are on a physiological, and not on a psychological basis. Abrupt withdrawal of alcohol after a period of 5 days of heavy dosage with resulting high average blood alcohol concentration produced paroxysmal slow activity in the EEG of one subject.

6. Electroencephalographic alterations associated with various experimental cardiac arrhythmias in dogs. — Edward Shev, Sanford E. Leeds and Harold Rosenblum, San Francisco, Calif.

The electroencephalographic changes noted in anesthetized dogs during the course of cardiac arrhythmia are to be reported in this paper.

These cardiac arrhythmias range from standstill to ventricular fibrillation.

The electroencephalographic changes are to be reported with the techniques we employed.

In the course of experiments on the effect of anoxia on the production of ventricular fibrillation and defibrillation, continuous simultaneous recordings of the electrocardiograph and the electroencephalograph were made.

Ventricular fibrillation was produced in two ways: (1) by low voltage electric shock and (2) by

temporary coronary artery occlusion. Defibrillation was carried out by the standard method of artificial respiration, cardiac massage and single or serial defibrillation shocks. The electroencephalogram was obtained with a standardized technique using a Grass III instrument. Needle electrodes were inserted in four areas of the scalp.

The resuls in fifteen experiments were essentially the same. There was a rapid loss of the brain wave pattern at the onset of ventricular febrillation. Upon defibrillation there was a return of the basic pattern, but with lower potentials.

The relation of these results to clinical cases of cardiac arrest will be discussed.

7. Alteration of simple performance with paroxysmal dysrhythmia. — CHARLES L. YEAGER and JOHN S. GUERRANT, San Francisco, Calif.

Paroxysmal activity in the EEG is frequently associated with impaired ability to function. By making simultaneous recordings of the EEG and the performance of volitional acts, such impairment has been demonstrated, whether or not a clinical seizure was involved. It was represented variably by changes in the accuracy or rate of performance or by total cessation.

The present study only roughly quantifies the degree of impairment and has considered only paroxysmal activity. The method employed, however, is adaptable to precise measurement and can readily be applied to any sort of discontinuous EEG activity, whether paroxysmal or not.

The demonstration and measurement of this impairment has important implications for the study of clinical conditions in which discontinuous abnormal EEG activity occurs, including mental deficiency, primary behavior disorders, criminality and antisocial reactions, as well as the convulsive disorders. It is expected, too, that these observations may be helpful in the study of the nature and composition of consciousness.

8. The electroencephalogram in anterior poliomyelitis. — A. A. MARINACCI.

Anterior poliomyelitis is considered to be a communicable disease. For this reason all the suspected cases in Los Angeles County area are sent to the Communicable Disease Unit of the Los Angeles General Hospital for screening. From February 1952 to October 1955 EEG's were taken on 4041 patients with either a suspected or confirmed diagnosis of anterior poliomyelitis. These EEG's have been reviewed according to age groups.

Group 1 consisted of 37 EEG's. Ages varied from 1 day to 11 months; 34 EEG's were normal and 4 EEG's were abnormal (8 per cent).

Group 2 consisted of 2082 EEG's. Ages varied from 1 to 10 years; 1819 EEG's were normal and 263 EEG's were abnormal (12 per cent).

Group 3 consisted of 726 EEG's. Ages varied from 11 to 19 years; 690 EEG's were normal and 36 EEG's were abnormal (5 per cent).

Group 4 consisted of 1196 EEG's. Ages varied from 20 years and over; 1150 EEG's were normal and 46 EEG's were abnormal (4 per cent).

Thus, the percentage of abnormality in 4041 cases was 9 per cent. The greatest abnormality was present between the ages of 1 to 10 years and was less in the adolescent and infant group and least in the adult group.

As one would expect the abnormality (delta activity) was more or less constant in patients with respiratory difficulty (bulbar). The abnormality was most likely the result of cerebral anoxia. The rest of the patients showed the variation on the EEG similar to that found in the normal population.

9. An experimental comparison of electroencephalographic patterns of normal and passive-dependent individuals. — SYDNEY KESSLER, Van Nuys, Calif.

Experimental purpose was to determine relationships between electroencephalographic patterns and passive-dependency. Two questions were: (1) Can the passive-dependency trait cluster be isolated and measured ? (2) To what degree does the cluster appear in specific populations ?

Psychiatric patients (Group H), diagnosed as passive-dependent by hospital psychiatrists and clinical psychologists, were compared to normal subjects (Group N). Each population of 110 subjects was administered a passive-dependency scale (*PD Scale*) and were measured electroencephalographically (EEG) for alpha index. *Scale* items were selected from authoritative sources.

Reliability coefficient .94 (Kuder-Richardson) for *Scale* items indicates internal consistency; eighty-six items at .01 confidence level, twenty-six at .05-.02 levels for a total 112 items (all by chi square). Groups H and N *Scale* means and sigmas are 50.45, 14.23 and 26.7, 15.04. EEG results, similarly, are 79.03, 11.5 and 62.32, 15.95. *PD Scale* and EEG *t* ratios are 11.99 and 7.04, at the .005 confidence levels.

Negligible Pearson *r* correlations appear for individual groups; .28 *r* occurs for combined populations. Significant .01 levels of curvilinear relationships (*eta*) occur for individual populations: .05-.02 when combined. Correlation ratios are: (1) Group H, .43 $\pm$ .09 PD against EEG; .52 $\pm$ .08 EEG against PD. (2) Group N, .37 $\pm$ .11 PD against EEG; .50 $\pm$ .10 EEG against PD. (3) HN combined, .36 $\pm$ .07 PD against EEG; .18 $\pm$ .05 EEG against PD.

Passive-dependency critical points, by converting ogives to straight-line prediction graphs, are 40 for the *PD Scale* and 72 for EEG alpha index. Either score suggests 50 per cent direction toward or away from passive-dependency.

Justifiable conclusions are: (1) Isolation and measurement of the passive-dependency trait cluster are objectively possible. (2) Diagnosed passive-dependent populations reveal significantly higher cluster incidence than normally distributed populations. (3) Electroencephalographic alpha index patterns measure passive-dependency as does the *Passive-Dependency Scale*. (4) By using *PD Scale* or EEG critical points of tendency, diagnostic determination of passive-dependency degree is feasible; both techniques increase reliability.

10. Color sensitivity in photoepilepsy. — KENNETH A. BLINN and DONALD B. LINDSLEY, Beverly Hills, Calif.

Previous studies by several authors have indicated the differential sensitivity, of humans and laboratory animals alike, to varying colors of flicker photostimulation. The clinical studies generally have emphasized the potency of the red end of the spectrum in eliciting electrographic responses, whether they be

seizure discharges in flicker-sensitive epileptics, threshold seizure bursts in Metrazol-activated patients, or merely visual cortex evoked potentials. The exceptions to this ''rule'' of red-sensitivity have stimulated speculation about inherent or constitutional differences in spectral sensitivity among photoepileptic patients.

With cognizance of the difficulties of controlling and evaluating the many variables of color photostimulation, the authors have attempted to systematize some observations on a small series of child and adult photoepileptics who were studied under widely varying parameters of stimulation. The techniques used have been exploratory rather than stereotyped, and the results therefore are not subject to over-all statistical analysis. Nevertheless, individual differences in susceptibility of patients to varying colors and varying modes of flicker stimulation have stood out clearly. In several cases, for example, blue-green sensitivity is demonstrated both electrographically and through the therapeutic efficacy of red-tinted spectacles. In addition to differential color presentation, a number of other techniques of stimulation have proved consistently fruitful, in hundreds of cases studied over the past several years. These include: the use of hemisected ping-pong balls as ideal neutral-tint diffusion goggles; electro-magnetic recording of finger-tapping during photo-evoked seizure discharges; and the ''glissando'' mode of varying flicker frequency.

11. The synchrony of alpha and beta activity recorded from bilaterally homologous leads by means of the double-beam oscilloscope. — B. Garoutte, R. B. Aird and T. E. Ogden, San Francisco, Calif.

Oscillographic recording at 50 centimeters per sec. (2 msec. per mm.) was performed on normal alpha (8-12/sec.) and/or beta (20-25/sec.) rhythms of 26 subjects.

In every one of the 24 cases where alpha rhythms were recorded bilaterally from occipital, central, or frontal areas, 25 to 90 per cent of all waves were perfectly synchronous, — i.e., within less than two milliseconds. The overall incidence of perfect synchrony was about 50 per cent. The waves which were not bilaterally synchronous were only very rarely more than 25 msec. out of synchrony.

In four patients where satisfactory recording of beta activity was possible, similar findings were observed. The delays never exceeded 17 msec. In any given subject from 20 to 60 per cent of the waves were synchronous, and the overall incidence of perfect synchrony was about 33 per cent.

In a group of 5 subjects chosen from the preceding group of alpha records, alpha activity was recorded from all cortical areas, so that delays between occipital and other portions of the cortex could be measured.

In contrast to the bilateral synchrony described above, this study of delays in the longitudinal direction revealed that the alpha peaks occurred in the occipital areas 15 to 20 msec. before central areas, and 40 to 55 msec. before the frontal areas in 3 of the 4 cases. In the fourth case, the delays were in the same direction, but smaller.

These data will be discussed as supporting the possibility of a central pacemaker for normal cortical rhythms, similar to that which has been postulated for abnormal rhythms.

12. Some properties of single epileptic neurons. — A. A. Ward, Jr., Richard P. Schmitt and L. B. Thomas, Seattle, Wash.

Using electrodes consisting of glass micropipettes, it has been possible to record the electrical activity of single cortical elements in chronic epileptic foci in both monkeys and humans. Unit activity of this type has been found to differ significantly from that observed in normals. Although the wave form of the individual action potential of an epileptic cell does not differ from that recorded in control experiments, the pattern of groupings of such discharges does show characteristic differences. The epileptic cell may discharge: (1) in brief, high frequency bursts at varying intervals in a relatively rhythmic fashion; (2) with prolonged, repetitive firing at 100-300 per sec. often preceded by a higher frequency burst; (3) in a more fully developed seizure sequence consisting of an initial ''tonic'' phase of continuous discharges up to 1,000/sec. followed by rhythmic bursts more or less in synchrony with the ''clonic'' spike of classical electroencephalography. The bursts of activity of a single cell show a variable relationship to the slower potential fluctuations such as would be recorded by a larger electrode. Although the data in the human is less extensive, for obvious technical reasons, the patterns of discharge of single cells in the vicinity of the epileptic focus in both man and monkey would seem to be much alike. In both species, the characteristic of the epileptic neuron is its propensity for autonomous discharge, often at very high frequencies, in contrast to the normal nerve cell.

One can postulate that the autonomous activity which characterizes the epileptic neuron is due to a difference in potential between the cell body and its dendrites. This could be due to a relatively enduring dendritic depolarization. The underlying cause of this potential difference might well be secondary to pathological changes in the dendrites in which mechanical deformation by the scar tissue could play a part.

13. The electroencephalogram in hepato-encephalopathy. — Walter J. Friedlander, San Francisco, Calif.

Serial electroencephalograms and measurements of blood ammonia were done in one patient with advanced Laennec's cirrhosis and in another with a surgically produced porto-caval shunt (Eck fistula). These measurements were obtained before and during the time the patients were receiving oral ammonium chloride. The administration of ammonium chloride was capable of producing the clinical signs seen during an exacerbation of their illnesses and a low protein diet could produce a remission of these signs. The blood ammonia level associated with a change in the electroencephalogram from normal to abnormal was 200-350 microgram/100 cc. Further details of the changes in the electroencephalogram and their correlation with blood ammonia levels and clinical signs are discussed.

14. Correlation between continuous determination of carbon dioxide level by infrared analyser with electroencephalographic findings; a preliminary report. — Leslie B. Mann, Leonard Wendland, Clarence Collier, Milton G. Crane and John Affeldt.

This paper presented the findings in 68 individuals of both sexes between the ages of 11 and 69 years

on whom continuous analysis of the alveolar carbon dioxide by means of a rapid infrared analyser was performed during the taking of a routine electroencephalography in the Outpatient Department of the White Memorial Hospital and the Respirator Center at Rancho Los Amigos. It was found that about one-half of the patients had some degree of "chronic" hyperventilation prior to the actual performance of hyperventilation. All factors responsible for this have not been determined as yet. In the typical alveolar carbon dioxide pattern the greatest drop of alveolar carbon dioxide level occurs within the first 30 sec. and although hyperventilation is continued for 3 to 4 min., changes in alveolar CO_2 levels beyond the first 30 sec. are rarely over 5 mm. of mercury. Because of the presently relatively small sampling it is not felt that definite clinical conclusions could be reached and the study is continuing, this paper representing a preliminary report on a method of simultaneous determination of the alveolar carbon dioxide and changes in the electroencephalogram.

15. Clinical and EEG correlations in cerebral palsy children and adults. — Donald B. Lindsley and Margaret Jones, Los Angeles, Calif.

One hundred and eighty cerebral palsy patients ranging from four months to adulthood have been studied clinically and electroencephalographically, some serially. Two-thirds of these are below eight years of age and one-half below 4 years of age. Several pairs of twins are included in the series.

One of the outstanding features occurring in approximately one-half of the children with cerebral palsy is the presence of a fast, rhythmic activity ranging from 15 to 30 per sec., and of voltage ranging from 5 to 50 μV. The frequency is usually 20 to 25 per sec. and is very rhythmic with amplitude modulations. The fast activity occurs in short isolated bursts or in continuing runs and is variously distributed, depending apparently upon the nature and location of cerebral damage, and bearing relation to clinical symptoms. The fast activity may become more prominent during light sleep or drowsiness, but not necessarily so. Most of our records were taken during the waking state and without sedation. The fast activity is best detected in bipolar records, although it may also be distinguished of course in monopolar leads, but is less apt to be detected.

Other types of abnormality, such as has been described by Perlstein, Gibbs and Gibbs, are noted as well, but these occur more frequently in association with convulsive symptoms and other evidences of focal pathology. Among 15 cerebral palsy adults, two-thirds or more have very even (flat except for alpha) tracings, with unusually rhythmic and unmodulated alpha activity.

These findings are interpreted in the light of recent neurophysiological findings, instead of in terms of traditional pyramidal versus extrapyramidal concepts as these have been related to spasticity and athetosis, respectively.

16. The EEG in severe speech and reading disabilities of childhood. — Eugene M. Webb and Lucie Lawson, San Francisco, Calif.

Electroencephalograms were obtained on 41 children who presented severe speech retardation or severe reading disabilities.

These 41 were selected from a group of 6 to 700 such children, on the basis that although the disabilities were severe and despite careful investigation, no other neurological, organic, emotional or intellectual impairment was uncovered.

Of the 41 encephalograms 24 were abnormal; 13 generally so, 11 with focal changes.

Among those with focal changes the most interesting was a 13 year old with a severe speech and reading deficit whose electroencephalogram showed a left temporal spiking focus. This child's identical twin had no disability and although her general electroencephalographic pattern was strikingly similar there was no spiking focus. The twin with the temporal lobe focus and the speech and reading disabilities was the second born and labor was difficult.

Although this small number must be regarded as a preliminary study, the high proportion of abnormal records suggests the possibility that an organic defect is responsible for the manifestations which is demonstrable by electroencephalography but not, at least readily, otherwise.

The original study was suggested because of the frequent observation that the degree of deficiency in reading in a given child varies greatly from day to day or even from hour to hour as though the deficit were intermittent or paroxysmal.

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Secretary: M. B. DELL

9 rue Jasmin, Paris XVI

1. Principles of photo-electro-nystagmography. — H. R. Richter, Basle.

The sensibility of the methods of registration based upon the recording of the variations of the ocular dipole has reached a limit with the routine equipment used at the present time, since the input energy remains constant and since the standard EEG equipment is being used in these studies at its upper limits of amplification. This is the reason which induced the author to develop a new photo-electric method which permits to increase the input energy. This is achieved by increasing the surface of the reflecting surface (illumination of the whole of the iris), by using a very powerful light source and finally by using two photo-electric cells with differential recording. This gives a sensibility which is about 10 to 20 times higher than that achieved with the ordinary methods of electro-nystagmography. At the same time the technique of recording of the eye movements is simplified. The photo-electric recording unit and the apparatus used to illuminate the eyes are mounted on goggles and the whole weighs no more than 500 g. Moreover the absence of electrodes simplifies the use of this device for the purpose of routine clinical examinations. A further advantage is that the head can be moved freely without producing disturbing artefacts and thus postural nystagmus can be studied easily.

The direction, the amplitude, the frequency and the duration of spontaneous nystagmus, postural nystagmus and nystagmus induced by the caloric test according to the method of Hallpike have so far been recorded in a very satisfactory way. The quantitative analysis of the ocular movements remains to be worked out in detail.

2. The mean potential of the EEG as a basis for the interpretation of cortical activity. — Z. Drohocki, L. Goldstein and B. Minz, Paris.

Quantification and codification of the EEG has been realized by using the integrator designed by Drohocki. The measures are represented in the form of chronological graphs and of statistical distributions. From this the ''position of the electrogenesis'', the slope of the variation and the direction of its change is determined at every instant. The results obtained in the awake rabbit show, that the amount of variability depends upon the duration of the successive periods during which the measurements have been taken. The more these periods are prolonged, the more constant the electrogenesis appears. The graph representing the electrogenesis becomes a straight line, which implies that there is a regulation of the amount of electrogenesis. There must therefore exist a *''constant of electrogenesis''*. This constant is characteristic for each individual and shows variations parallel to physiological changes in brain activity. This constant constitutes the basis for ''cerebral electrometry''. The statistical distributions of the potentials are normal. The deviations from the value of the constant, which are identical with the ordinary oscillations of the EEG do not trespass the limits of such a statistical distribution and are therefore accidental. It is therefore important to study the parameters of the ''constant of electrogenesis'' since this is the more significant phenomenon than the instantaneous variations of the EEG.

3. The quantitative differences in the EEG of the rabbit during wakefulness and narcosis. — Z. Drohocki, L. Goldstein and B. Minz, Paris.

The method of quantitative analysis of the EEG with the integrator of Drohocki is well suited for investigations in cerebral pharmacology. The authors used it for a comparative analysis of the action of ethyl-urethane in the rabbit. It was attempted to determine up to what point this anesthetic produces a state of stability in the cortical electrogenesis. It is indeed of great importance to define as accurately as possible a measure, which can be used as a baseline for further investigations. It became apparent, that contrary to the accepted views, ethyl-urethane anesthesia produces a very marked instability. One observes a great fluctuation in electrogenesis with periods of very variable output successing each other at brief intervals. On the other hand, as described in the previous communication, the electrogenesis during wakefulness is characterized by its great stability. It appears therefore logical to take it as the baseline.

4. The action of adrenaline upon the cortical activity of the rabbit. — Z. Drohocki, L. Goldstein and B. Minz, Paris.

The findings obtained by Goldstein and Minz according to which there is an exponential increase in electrogenesis following an intraveinous injection of a very small amount of adrenaline (1 cc. of 10^{-5} per cent sol.) in the rabbit under ethyl-urethane anesthesia were verified and analysed with the integrator of Drohocki. The adrenaline was given in the same way as in the original experiments. The results have confirmed the previous findings, i.e. the exponential character of neuronal recruitment under these conditions. This implies the existence of a system, in which the number of active neurones doubles at every instant.

5. An electrophysiological study of the reflex excitability of motoneurones in man. — J. Paillard, Paris.

The authors make use of the possibility to elicit by electrical stimulation in man a reflex response of motoneurones (Hoffmann's reflex). The electrical stimulation under these conditions gives an opportu-

nity to evaluate the excitability of the spinal motoneurones (monosynaptic test). The authors have worked out the experimental basis allowing a precise application of this method for human clinical neurophysiology. The important points are: fixation of the limb, electromyographic record, stabilisation of the stimulation and clear definition of the parameters of stimulation (duration, intensity and "cadence"), checking of the subliminal fringe, checking of the level of excitability. The authors proposes different criteria which were tested in 30 normal subjects and which seem to be useful in clinical medicine: (1) curves comparing the variations in amplitude of the reflex and of the primary response as related to the intensity of stimulation; (2) excitability curves of the motoneurone (already utilized by Magaladery and coll. in 1952), which become more informative when taken under various conditions of central recruitment and which should be compared with the mechanogram of the reflex contraction; (3) effects of the modification of the stimulation "cadence" upon the amplitude of the reflexes; determination of the optimal "cadence" of recruitment (experimental clonus) and of the "zones de battements"; (4) effects of passive movements of the extremity upon the excitability of the motoneurones.

The interpretation of the informations thus obtained is discussed in the light of our present knowledge of the function of the motoneurone and the muscular proprioceptors. The interest to extend this type of studies to include the investigation of the physiopathological mechanisms of certain motor disorders is stressed.

References: PAILLARD, J. *J. Physiol.*, Paris, **1953**, *45*: 206; **1954**, *46*: 484. *Pflügers Arch.*, **1955**, *260*: 448; Thèse Faculté de Sciences, Paris, **1955**. Réflexes d'origine proprioceptive chez l'homme, 314 pp.

6. Demonstration of the existence of a mechanism regulating the sensibility of the intramuscular tension receptors (muscle spindles) in man. — J. PAILLARD, Paris.

The comparative study of reflexes obtained by percussion of the tendon and by electrical stimulation of the nerve permit to extrapolate to man the findings in animal physiology concerning the central pathways of the myotatic reflex. The systematic comparison of the responses obtained by both methods of investigating the reflex excitability constitutes a differential test, which allows to differentiate between the effects which are exerted upon the muscle spindles and those acting directly upon the excitability of the motoneurones. This method makes it possible to demonstrate the importance of a particular type of regulation involving specifically the tension of the intrafusal myofibrils. This regulation mechanism influences the tendon reflex, but does not modify the electrically elicited reflex.

Recent findings in animal neurophysiology suggest that the influences acting upon the motor apparatus of the muscle spindles are mediated by the small type of efferent fibers (gamma efferents). It would be of interest to apply these methods of investigation to clinical problems and to the investigation of the pathology of the mechanisms regulating the tonus of the muscle spindles.

7. Reflections on the mechanism of the action of hyperventilation upon the EEG. — M. BONVALLET and P. DELL, Paris.

The accepted theory concerning the effect of hyperventilation upon the EEG was, that these effects were due to hypocapnia inducing secondarily circulatory changes in the cerebral cortex. In a recent experimental study the authors have demonstrated that an increase of the CO_2 pressure in the blood produced an excitatory effect upon the ascending activating reticular formation (AARF) and by this produced cortical arousal. The reticular formations are directly influenced by the blood CO_2. An adequate CO_2 pressure is an essential condition for the normal functioning of the mesencephalic reticular formation as it is notoriously for the bulbar reticular formation which regulates respiration.

Hypocapnia produced by hyperventilation diminishes the activity of the AARF and in certain individuals it even suppresses its function. It is well known, that the activity exerted by the AARF normally inhibits spindling (recruiting system) and slow waves (delta waves). These two types of activity are released of their reticular inhibitor under hypocapnia as they are when the activity of the AARF diminishes when one drops asleep. The slow waves appear due to a similar mechanism both during hypocapnia and during drowsiness deepening into sleep. Moreover it is well known, that the diminution of the activity of the AARF tends to activate epileptic discharges, though the intimate mechanism of this activation still remains obscure. On the other hand this tendency to epileptic activity is often suppressed by substances, which intensify the activity of the reticular formation (CO_2, amphetamine, etc.).

8. EEG findings during experimental surgical interventions upon the exsanguinated heart under hypothermia. — G. ESPAGNO and CH. GRÈZES-RUEFF, Toulouse.

It is an accepted view that the brain is unable to sustain without damage to be deprived of blood for a period longer than 5 minutes. The authors wanted to determine, if under hypothermia this period of tolerance could be extended.

The electrical activity of the brain was observed by means of electroencephalographic recordings during the different stages of anesthesia and hypothermia. The recording of the EEG was continued during the interruption of blood circulation and the delays of disappearence of electrical activity of the brain following this interruption were observed. Total cerebral anemia was always maintained for 15 to 20 min. Such an anemia seems to be well tolerated by the brain under hypothermic conditions at 24-28° C.

In many cases the delay with which electrical activity of the brain reappeared after the blood circulation was reestablished could be observed. This recuperation time was very variable (several minutes to several hours) and its duration appears to be in relation to a certain degree with the method used to induce hypothermia. Especially the use of too many various drugs seems to have a detrimental effect, since they all exert a depressive action.

It follows from these observations, that under hypothermia the brain is capable to sustain absolute anemia for 15-20 minutes, instead of 5 minutes as under normothermic conditions. A seemingly normal electrical activity together with normal behavior was observed in dogs following a period of several hours

during which the cerebrum did not show any trace of electrical activity.

9. Electromyography in Parkinsonism (A report on 70 cases). — F. Thiebaut, F. Isch, Mme. Isch-Treussard and J. Jouffroy, Strasbourg.

In 70 Parkinsonian patients with different durations of their illness, different etiology and symptomatology an electromyographic study was carried out which consisted in recording at different times in the same patient the electrical activity of flexor and extensor muscles of the fingers. These records from the two muscle groups were recorded simultaneously at rest, during voluntary movements and during passive movements of extension and flexion of the wrist.

These electromyographic studies gave the following results: (1) at rest: either the different forms of tremor were seen, or a continuous activity in both muscular groups or only in one, usually in the extensors or finally electrical silence. (The authors think that the akinetic state is rather due to a blocking of voluntary impulses than to an involuntary contracture inhibiting the automatic movement; (2) during voluntary movements: frequently disturbances of reciprocal innervation were observed; (3) during passive movements: the frequent occurrence of lengthening reactions was noted and especially the occurrence in the majority of cases of a burst of activity when the shortening of the extensors was released. These phenomena seem to be most common expression of the disturbances of extrapyramidal tonus (plasticity).

On the basis of these electromyographic criteria the therapeutic action of various treatments could be evaluated.

10. Guanidine and myasthenia gravis. — J. E. Desmedt, Brussels.

The author studied, as Minot, Dodd and Riven in 1939, the action of guanidine in a series of patients suffering from myasthenia gravis. In all cases this chemical compound produced a significant improvement as mesured with dynamometric and ergographic tests and as evidenced by the reduction or even complete disappearence of the signs of neuromuscular depression revealed by the electromyographic responses to electrical stimulation. The therapeutic use of guanidine produced good results in a certain number of cases. The mechanism of this action was discussed and a comparison made with the mode of action of other drugs used to remedy the symptoms of myastenia as e.g. potassium and anti-cholinesterases.

11. Pentothal anesthesia and brain stem. — J. Schneider and G. Thomalske, Colmar.

The authors discuss in the light of present neurophysiological knowledge: (1) the role which subcortical formations regulating the electrical activity of the cerebrum play for the development of the different electrographic stages of anesthesia; (2) the pathways by which the influences exerted by these structures act upon the cerebral cortex.

12. A pharmacological method of investigating cortical and subcortical function in man and its electrographic criteria. The localisation of lesions with the Pentothal method. J. Schneider and G. Thomalske, Colmar.

The authors study the possibilities offered by the method of injecting Pentothal in order to disclose latent electrographic abnormalities and to localise a pathological intracranial process, especially lesions destroying or compressing subcortical centers regulating the electrical activity of the cerebrum or their projection pathways to the cortex.

The results of such studies carried out in 360 subjects suffering from various cerebral diseases, 117 of them tumors, are reported. In all cases the localization of the lesions was verified either at operation or at autopsy or with standard neurosurgical methods.

13. The electrical activity of the brain in mature and premature newborn infants. — C. Dreyfus-Brisac, D. Samson and N. Monod, Paris.

The recording of the EEG in newborn infants and premature babies has allowed to determine the normal patterns of electrical activity for the different fetal ages mesured from the time of conception. The EEG shows a discontinuous activity up to the fetal age of 8 months.

At the fetal age of 5 months: diffuse discharges of slow waves occurring in bursts at a frequency of 1 c/sec. of high amplitude and sequences of rapid rhythms at 4-6 c/sec. and 8-12 c/sec.

At the fetal age of 6 months: 5 c/sec. waves occurring in bursts which are synchronized over one hemisphere.

At the fetal age of 7½ months: bursts of 1-2 c/sec. waves with superimposed more rapid rhythms with predominance in occipital areas and occurring already in a more continuous fashion.

From the 8th fetal month on the EEG shows continuous electrical activity of the brain and resembles the activity recorded in newborn infants born at full term. There already exists a slight differentiation between a wake and sleep pattern.

The development of the electrical activity is quite rapid and is a function of the time elapsed since conception. The EEG tracing of a premature baby which has reached the age of the full term and that of the newborn born at that term are essentially identical. The maturation process therefore seems to be independent from the date of birth.

The discontinuous character of the electrical activity of the brain previous to the 8th fetal month, its very rhythmical character, certain of its characteristics of distribution (particularly the synchronization of this activity over one hemisphere and the hemispherical asynchrony at the fetal age of 6 months) suggest that these rhythms seen in premature babies born at a very early fetal age are not of cortical origin. Anatomical, chemical and cytological data (Flexner, Krebs), electrographic data gained from thalamic recordings (Jasper, Hunt, Bishop, Sherrer and Oeconomos), as well as experimental data (Morrison and Basset, Meyers and Knott) and especially the study of decorticate animals and the recording of bursts of rhythmical activity in the nucleus caudatus (Kennard) seem to support this hypothesis.

14. The reactivity of the EEG in infants. — C. Dreyfus-Brisac, C. Blanc and P. Kramarz, Paris.

The topographical distribution of the diffuse responses in the EEG occurring during deep sleep has been studied in infants in respect to the pathways mediating these responses. Children from the

newborn age up to the age of 2 years were thus investigated.

The monopolar analysis of these diffuse electrographic responses shows that there are three types of such responses: frontal, central-vertex and occipital. Maximum amplitude is recorded in posterior head regions. Sharp waves are the most common form of response in central regions. These phenomena become particularly clear from the age of 1 year onward.

The existence of different morphological types of responses in different cortical areas raises the question as to how the subcortical structures of the diffuse projections system are connected with the cerebral cortex. These relationships are very complex. They seem to be related to different anatomical systems which are functionally distinct from each other. In infants the projection to the cortex of responses mediated by the thalamic association nuclei seems to be a hypothesis worth considering. The thalamocortical systems involving the pulvinar and the temporo-occipital cortex on one hand and the anterior thalamic nuclei and the cingular gyrus on the other seem to play an important role in the transmission of diffuse electrographic responses to the occipital and central vertex region. There are numerous EEG findings which indicate the functional importance of these systems in the organization of the cerebral activity in the infant.

15. The conditions of appearance and the statistical importance of the lambda waves in normal subjects. — A. Rémond and N. Lesèvre, Paris.

The positive spikes of the occipital region were first observed by Evans in 1949 and described by Y. Gastaut in 1951. Evans in 1953 found them in 2 per cent of his subjects. In the same year M. Roth and J. Green observed them in 60 per cent of their subjects.

In recent studies of normal subjects the authors found these spikes in 61-99 per cent of all investigated subjects. These wave forms were less frequently seen in a group of individuals with a regular and rather slow alpha rhythm, which was rarely desynchronized and only moderately reactive (group I). On the contrary this phenomenon was always encountered in subjects with a not very well synchronized background activity of complex form and which proved to be very reactive (group II).

The difference between these two groups may explain the differences in the statistical evaluation of the frequency of the occurrence of lambda waves as apparent from the studies of the authors cited above. The following criteria should be emphasized: (1) from the technical point of view it is important to use high gain recordings, since these lambda waves very often are of very low amplitude (about 10 μV. or below). They are frequently seen wiht gains of 5 μV./mm. They are almost always seen with gains of 2.5 μV/mm. They are recorded only from occipital electrodes; (2) the lambda waves do not appear in darkness, even when the subject opens and closes his eyes. In a bright laboratory they appear in 14 per cent of the cases on simple opening of the eyes, but become much more prominent, if the subject looks with intention, i.e. actively performs a visual analysis of an object. They are best seen when this object is complex and able to arouse interest. They are minimal or even absent for objects which are too simple or not capable to arouse any interest. The plates 18 B and 13 M F of the T A T test e.g. produced quite conspicuous lambda waves. The plate 14 made them disappear, even when they were present spontaneously. Finally one sees lambda waves during projection of a movie or during reading, but a close correlation between the moment of their onset and their number on one hand and the degree and number of eye movements on the other could not be established.

16. The modifications of the electrical activity of the rhinencephalon and the thalamus in animals under the influence of oestrogens and adrogens. — J. Faure and J. Gruner, Bordeaux and Paris.

The experimental animals (22 female rabbits, 7 albino mice and 10 guinea pigs) were alert and kept in cages. Acute and chronic preparations with fine bipolar electrodes in the olfactory nucleus, the fornix, the hippocampus, the reticular formation of the mesencephalon, the medial geniculate body, and the thalamic reticular nucleus received small, medium and high doses of sex hormones.

Oestradiol produced in the following preferential order a hyperactivity of the mesencephalic reticular formation, the hippocampus, the fornix, the olfactoseptal formations together with an enhancement of thalamic synchronization. Histamine facilitated this action and displaced the maximum of the hyperactivity towards the anterior rhinencephalon.

The androgen from the adrenals produced a lasting thalamic synchronization, testosterone bursts of synchronization and glycosteroids a desorganization of the electrogram.

Two successive phases of behavior were observed: ''hypersyntony'' with aggressiveness followed by automatic ''oral'' activities. The second phase was sometimes followed by hippocampal seizures in acute preparations or by an abnormal sexual behavior in the chronic animal. This general type of behavior showed secondary modalities depending upon the hormone used. The respiratory rhythm was altered, when spindles (folliculine) or synchronized bursts (testosterone) appeared.

It is felt that these hormones exert an influence upon an olfacto-septal and mesencephalic system on one hand and a hippocampo-thalamic system on the other.

17. A comparison of the EEG with hormonal changes in female patients. — J. Faure, J. Magendie, E. Boussemart and M. Masquelier, Bordeaux.

The EEG of 250 female patients suffering from gynecological and endocrine conditions were grouped according to common electrographic signs. The hormonal titer of 70 out of 250 of these patients were then determined.

It was possible to describe 5 types showing correlations between electrographic and endocrine signs.

I. *Dominant hyperfolliculinemia.* Mixed rapid and slow activity (folliculine +), predominant rapid activity (F.S.H. +), rhythmic discharges in bursts (17-K.S. +), disorganization (11-oxysteroids +).

II. *Hyperluteinism.* Rare bursts of polyrhythmic discharges on a reduced background activity.

III. *Hormonal deficit.* High amplitude slow waves (pure deficit), burst of rhythmical discharges (17-K.S. +), disorganization (11-oxysteroids +).

IV. *Spontaneous menopause.* Very rapid rhythms (F.S.H. +), bursts of rhythmical waves (17 K.S. +).

V. *Castration syndrome.* Bursts of rhythmical discharges (17 K.S. +), desorganization (11-oxysteroids +).

An excess amount of 17-ketosteroids or of 11-oxysteroids was accompanied by a typical EEG pattern. The behavior was the same in all these conditions: anxiety with affective disturbances, lack of or difficulty in contact with the patient's milieu, abnormal viscerosomatic sensations, automatisms and inhibitions. The predominance of a certain element produced a certain type of behavior, which was in relation with the curve of excitability and the hormonal titer. Respiratory disturbances were constant. These findings were used as a basis for therapeutic procedures.

18. Contribution to the electroencephalographic study of endocrine syndromes. — F. Thiébaut, F. Rohmer and E. Wackenheim, Strasbourg.

The authors present an EEG study of seven groups of endocrine disorders. After having reviewed the pattern of the EEG response to hypoglycemia provoked in normal subjects they report on two cases of electrographic hypersensibility to hypoglycemia. Then the EEG seen during insulin treatment with the method of Sakel is described, as well as that of posthypoglycemic coma and of hyperinsulinism.

In the group of tetanies they distinguish three types of EEG patterns: that seen in hypoparathyroidism with convulsions and hypocalcemia, that in neurogenic tetany and finally a mixed group with cases of hypoparathyroidism and "spontaneous" tetany.

The endocrine disorders of the thyroid glands produce very different EEG patterns depending upon the nature of thyroid dysfunction. The EEG patterns of hypo- and hyperthyroidism are quite different. Besides those very well known differences the authors distinguish the pattern seen in primary from that seen in secondary hyperthyroidism (according to the classification of F. Thiébaut).

The analysis of the EEG records in patients suffering from a hyperfunction of the adrenal cortex shows that the electrogram is often abnormal, but any significant correlations cannot be established. These patterns however resemble very much those seen in acromegaly. Adreno-cortical insufficiency produces electrical abnormalities, which can be aggravated by administration of desoxycorticosterone, when this hormone is not given together with cortisone.

Cases of acromegaly and acromegaloid syndromes are interesting to study, for the pattern correlates quite well with the progressive growth of the adenoma or with its regression under the influence of X-ray therapy.

Among the endocrine syndromes of hypothalamic origin the authors studied the following ones: (1) Froehlich's syndrome were the tracing is borderline normal in adults. In adolescents however two types of patterns can be distinguished according to the post-encephalitic or "degenerative" origin; (2) Diabetes insipidus, in which the EEG is essentially undisturbed, except for occasional rapid activity; (3) the "hemorrhagic" fibroma of the masculine puberty; (4) the hypothalamic amenorrheas.

In the group of the cranial hyperostoses due to endocrine disorders the authors distinguish on one hand the internal frontal hyperostosis, which is often associated with rapid activity in anterior head regions and on the other hand the "diffuse cranial osteosis", which quite to the contrary is associated with diffuse slow waves.

19. The EEG in mental retardation, mental deterioration and alert confusion. — G. C. Lairy, J. Rallo and H. Boutillier, Paris, Bonneval.

The EEG study of mental deteriorations gives a chance to evaluate how the electrographic pattern adapts itself to a irreversible deficit and how this deficit is reflected in the EEG. The records are evaluated according to the degree, the nature and the evolution of the deficit. The EEG investigation of cases with alert confusion discloses the effects of momentary disturbances in contact with the outside world upon the wake brain rhythms and their reactivity.

The differences and the similarities of the EEG aspects in these two clinical groups are discussed.

20. The significance of the alpha rhythm in psychiatry. — G. Daumézon and G. C. Lairy, Paris.

The alpha rhythm and its mode of appearance and blocking are evaluated in connection with the global attitude of the patient in his contact with his environment.

In mental patients in which the difficulties in contact with their surroundings are the dominant pathological phenomenon, one can observe different degrees of disturbances of the alpha rhythm and its reactivity: (1) an abnormally long latency of the arrest reaction, followed by a momentary reinforcement of the alpha activity; (2) reappearence of alpha activity on a flat background in response to some stimulation (relaxation response or arousal response); (3) increase of the threshold of reactivity; (4) extreme lability of the wake rhythms alternating with sleep potentials.

The notion of "abnormal rhythms" should be replaced by that of functional disturbance of their dynamics, an interpretation close to that applicable to the clinical symptomatology.

21. EEG studies in manic-depressive psychosis. Methodological considerations. — Th. Kammerer, F. Rohmer, L. Israel and A. Wackenheim, Strasbourg.

The authors report on an electrographic and clinical study of manic-depressive psychosis, melancholy and mania. They point out the frequent occurrence of quite conspicuous abnormalities, which were much more often seen than might have been expected on the basis of previous reports. Certain EEG characteristics are found in a high proportion of cases, especially the rapid disturbances.

The authors also point to the specific difficulties inherent to the use of EEG in psychiatry and indicate certain measures of precaution which may help to eliminate numerous sources of errors.

22. EEG studies in some cases of cerebral herniations, some accompanied by brain stem lesions. — J. Le Beau and M. Dondey, Paris.

The authors review a small series of cases with cerebral herniations associated with various hemispherical and brain stem lesions which were anatomically and histologically verified.

In view of the polymorphism of the electrical alterations related to the underlying disease process responsible for the herniation, it seems impossible

to point to any electrographic signs, which might be characteristic for brain herniations. However the combination of such herniations with brain stem lesions reflects in the EEG pattern. In the alert subject in the relaxed state this is manifest by the presence of theta rhythms varying in rate between 5 and 6 c/sec., showing a regular wave form and symmetrical distribution especially in anterior head regions.

23. A case of temporal lobe epilepsy in a hypoglycemic patient. — J. GACHES and M. DONDEY.

The case of a patient is reported, who for 5 years showed manifestations of hypoglycemia and temporal lobe involvement (generalized convulsions preceded by muscular aches, a fainting sensation, followed by a state of confusion and speach disturbances).

Many records were taken, which showed: (1) anterior temporal abnormalities on the left side with no signs indicating the presence of a superficial focus (slow waves with sharp wave front, paroxysmal bursts of theta waves, irregular or regular spike and wave complexes). These signs were quite variable; (2) signs attributed to a very mild hypoglycemia of unknown origin, though attempts were made to explain it by carrying out endocrinological tests.

The EEG manifestations of this hypoglycemia though quite ordinary in their form were quite remarkable for other reasons. Provoked hypo- and hyperglycemia carried out during EEG examinations showed that this was not only a simple juxtaposition of the two related EEG phenomena, but represented a true activation of the temporal abnormalities by hypoglycemia.

This case was presented for the following reasons: (1) because of the minor character of the hypoglycemia, which could easily have been overlooked; (2) because of the association of the electrographic signs due to the hypoglycemia with the left temporal abnormalities appearing at a moment when the blood sugar was at about 0.65 gr. and because of the intricate interrelationships of the clinical signs, on the basis of which it is at times difficult to decide which are the effects of temporal lobe disturbances (postictal speech difficulties) and which are those due to hypoglycemia (slowing of mental processes, pallor, sweating); (3) because of the therapeutic problems involved in a case of association of such disturbances; (4) because of the interest to use the provoked hypoglycemia test as a method of activation of the EEG.

24. Epilepsy and postoperative course of 31 cases of brain abscess. — Mme. A. ZALIS and Mme. G. ARFEL-CAPDEVIELLE, Paris.

The authors first discuss the general conditions of appearance of post-operative epilepsy in cases of brain abscess. In 31 operated patients 20 developed epileptic seizures. The majority of these attacks began wihin the first 2 years after the operation. The importance of the age of the patient could not be clearly established.

The frequent occurrence of seizures is then discussed in respect to the anatomical location of the lesions. Cerebellar abscesses did not produce postoperative epilepsy. In frontal abscesses there were surprisingly less postoperative epilepsies than in other hemispherical abscesses. Patients which were treated by simple puncture developed seizures more frequently than those in which the abscess was excised in toto. Two cases of subdural empyema and of pyogenic inflammation of the cortex and overlying pia did not develop seizures.

Finally the importance of the bacteriological factors is considered. Sterile abscesses have proved to be just as epileptogenic than others, but the abscesses due to anaerobic germs have always produced seizures. From the electrographic point of view it is worth mentioning that the alpha is sometimes depressed on the operated side; at others, however, augmented in amplitude with a tendency to progressive increase in amplitude. There is always irregular delta activity in the region of the bone flap during the first three postoperative weeks, but this slow activity regresses more or less rapidly. However, irritative phenomena and spike discharges behave differently, they progress in contrary. The minor changes, such as rapid rhythms, sharp waves and theta activity, are more frequently seen in epileptics than in patients, which remain seizure free. Their diagnostic value is even more important, when one considers that true spike discharges are present only in one out of two patients. The presence of a well circumscribed spike focus is a valuable criterion in evaluating the advisability of an operation.

25. Pre- and post-operative studies of electroencephalographic signs of brain abscesses. — CL. SALLOU, Paris.

This study deals with 40 cases of brain abscess surgically or anatomically verified.

Ninety-eight per cent of the cases of brain abscess have an abnormal EEG. There is a quite close correlation between the electrographic signs and the pathological state of development of the abscess. The irregular focal delta is good localizing sign, still less reliable however than the neuro-radiological signs. Too great a discrepancy between electrographic signs and clinical symptomatology suggests the possibility of multiple abscess.

The postoperative electrographic abnormalities are very persistent. In 47 per cent of the cases epileptic seizures with focal onset are observed. The long range results are no different from one method of surgical treatment to another. The frequency with which these postoperative seizures occur is probably related to irreversible lesions of nerve cells which occurred already before operation.

Reference: Cl. Sallou, Thesis. Paris, February 1954.

26. Unusual electrographic signs consecutive to head injuries. I. Bilaterally synchronous discharges of multiple spike and wave complexes provoked by intermittent photic stimulation (I.P.S.). Their relation to posttraumatic epilepsy with generalized convulsions. — H. GASTAUT and P. NARAVANNE, Marseille.

The authors report on 14 cases of multiple spike and wave discharges provoked by intermittent photic stimulation in patients having suffered from head injuries and complained of banal subjective symptoms. They are compared with 7 cases with identical discharges, which were provoked in the same manner, but the patients suffered from posttraumatic epilepsy of the grand mal or petit mal type. The practical and theoretical importance of these cases is discussed. The generalized convulsions occurring after head injuries are of "centrencephalic" origin. The medico-

legal significance of the discharges observed in non epileptics is not very great.

27. Unusual electrographic signs consecutive to head injuries. II. The posterior rhythms at 4 c/sec. — M. PITOT and H. GASTAUT, Marseille.

The authors report 12 cases showing electrographic abnormalities apt to be encountered in sequelae of head injuries. It consists of a rhythm at 4 ± 0.5 c/sec. superimposed upon the alpha rhythm in parieto-occipital and temporal areas and reacting as the alpha rhythm does to eyes opening, mental calculation and to intermittent photic stimulation. On the other hand this rhythm is modulated in an independent fashión over the two hemispheres and is therefore seen to occur in asymmetrical and asynchronous bursts.

The patients showing this abnormality usually complain only about the usual subjective symptomatology of a banal type so frequently encountered after head injuries. It is however possible that hypothalamic signs may complicate the picture. They consist of hypothalamic amenorrhea, loss of weight or obesity, sleep disturbances, etc. It seems therefore that this represents a mesencephalo-diencephalic disturbance caused by the head injury, possibly related to a contre-coup lesion. Similar disturbances are seen in other lesions of the basal formations of the brain, especially in the sequelae of tuberculous meningitis.

28. EEG observations in a case of Fahr's disease. — S. THIRY, Liège.

The author reports EEG findings and clinical and anatomical data of a case showing idiopathic intracerebral vascular calcifications not due to arteriosclerosis (Fahr's disease). The pertinent litterature is reviewed.

29. Convulsions with hypocalcemia in a 7 months old baby. Persistence of electroencephalographic and neurological signs despite return to a normal blood calcium concentration. — M. BONDUELLE and CL. SALLOU, Paris.

The authors report the case of a 7 months old baby, who without any preceding illness went into status epilepticus with a hypocalcemia at 54 mg. The child was followed up from the electrographic and clinical point of view. The calcium level returned very rapidly to normal. However the focal EEG alterations persisted in serial EEG studies and the neurological signs also failed to disappear.

The diagnosis and prognosis is discussed.

30. The use of filtering glasses in photosensitive epilepsy. Theoretical and practical considerations. — J. LEBASCLE, Casablanca.

The author who studied the effect of filters of different colors upon the abnormalities produced by intermittent photic stimulation in cases of photosensitive epilepsy, noticed a disappearence or marked attenuation of these abnormalities with polaroid glasses of a green color or with glasses called "filtrays C".

These glasses absorb electively an important fraction of the red rays of the visible spectrum.

The author taking up a hypothesis proposed by Symnes and Carterette thinks, that these glasses act by selective filtering of the red rays rather than by producing overall attenuation of the light intensity. Practical consequences derive from these observations.

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